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STRUCTURE FILE UPDATES: 14 NOV 2004 HIGHEST RN 780728-63-4 DICTIONARY FILE UPDATES: 14 NOV 2004 HIGHEST RN 780728-63-4

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

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NODE ATTRIBUTES: DEFAULT MLEVEL IS ATOM DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES: RING(S) ARE ISOLATED OR EMBEDDED NUMBER OF NODES IS 17

STEREO ATTRIBUTES: NONE L2 8939 SEA FILE=REGISTRY SSS FUL L1

100.0% PROCESSED 16595 ITERATIONS SEARCH TIME: 00.00.01

8939 ANSWERS

=> d sta que 15 L3 STR

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NODE ATTRIBUTES: DEFAULT MLEVEL IS ATOM DEFAULT ECLEVEL IS LIMITED

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NUMBER OF NODES IS 10

STEREO ATTRIBUTES: NONE

L5 4726 SEA FILE=REGISTRY SSS FUL L3

100.0% PROCESSED 102951 ITERATIONS

SEARCH TIME: 00.00.08

4726 ANSWERS

=> d his

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SET COST OFF

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L1 STR

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L3 STR

L4 46 S L3 L5 4726 S L3 FUL

SAV L5 NEON402B/A

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L6 101 S L2 AND L5

L7 20 S L6 AND (PD<=19970213 OR PRD<=19970213 OR AD<=19970213)

L8 3 S L7 AND (MAZESS ? OR BISHOP ?)/AU

L9 3 S L7 AND (BONE(L)CARE?)/PA,CS

L10 3 S L8,L9 SEL HIT RN

FILE 'REGISTRY' ENTERED AT 10:25:11 ON 16 NOV 2004

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L12 4 S L11 NOT L2

L13 ' 28 S L11 AND L5 L14 24 S L13 NOT L12

L15 36 S L11 NOT L12-L14

L16 0 S L15 AND (P AND N)/ELS

FILE 'HCAPLUS' ENTERED AT 10:26:20 ON 16 NOV 2004 SEL RN L10

FILE 'REGISTRY' ENTERED AT 10:26:24 ON 16 NOV 2004

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98 S E65-E162
L17
             34 S L17 NOT L11
L18
              3 S L18 AND (P AND N)/ELS
L19
              2 S L19 NOT CO/ELS
L20
L21
              6 S L12, L20
                SEL RN
L22
            115 S E163-E168/CRN
L23
              0 S L22 AND L2
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           2059 S L21 OR L22
L24
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L25
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L26
L27
           8028 S L24-L26
L28_____111_S_L27_AND_L2___
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L30
             3 S L10 AND L29
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              6 S L31 AND E169-E186
L32
L33
             23 S L31,L32
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L34
           7500 S L27
L35
           1410 S L2
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L39
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              6 S L39 NOT P450/TI
L40
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FILE 'REGISTRY' ENTERED AT 10:41:02 ON 16 NOV 2004

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FILE COVERS 1907 - 16 Nov 2004 VOL 141 ISS 21 FILE LAST UPDATED: 15 Nov 2004 (20041115/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN

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AN
    2003:532131 HCAPLUS
DN
    139:101329
ED
    Entered STN: 11 Jul 2003
TI
    Targeted therapeutic delivery of vitamin D compounds
IN
    Mazess, Richard B.; Bishop, Charles W.
PA
    Bone Care International, Inc., USA
SO
    U.S. Pat. Appl. Publ., 28 pp., Cont.-in-part of U.S. Ser. No. 402,636.
    CODEN: USXXCO
DT
    Patent
    English
LA
IC
    ICM A61K039-395
    ICS A61K031-727; A61K031-66; A61K031-59
    424178100; 514102000; 514167000; 514054000; 514056000
NCL
    32-7 (Steroids)
CC
    Section cross-reference(s): 29, 63
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                              DATE
                                          APPLICATION NO.
                                                                DATE
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                                          US 2003129194 A1
                              20030710 US 2002-251905
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                              19980820
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            GA, GN, ML, MR, NE, SN, TD, TG
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PRAI US 1997-38364P
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                        W
                              19980213
    US 2000-402636
                        A2
                              20000426
CLASS
PATENT NO.
                CLASS
                      PATENT FAMILY CLASSIFICATION CODES
US 2003129194
                ICM
                      A61K039-395
                ICS
                      A61K031-727; A61K031-66; A61K031-59
                      424178100; 514102000; 514167000; 514054000; 514056000
                NCL
                      A61K047/48H4; A61K047/48T8M4
US 2003129194
                ECLA
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ECLA

WO 9835704

GΙ

AB The present invention is directed to a conjugate which includes at least one vitamin D moiety and at least one targeting mol. moiety to pharmaceutical compns. of the conjugate, and to methods for using the

Ι

A61K047/48H4; A61K047/48T8M4

```
conjugate for target-specific delivery of vitamin D or analogs to tissues.
     When a particularly preferred form is administered to a patient, the
     targeting mol. component of the conjugate of this invention seeks out and
     binds to a tissue of interest, such as bone or tumor tissue, where the
     vitamin D has a therapeutic effect. One example compound prepared was I.
ST
     vitamin D phosphonate deriv prepn targeted delivery
TT
     Antitumor agents
     Bone
     Drug delivery systems
     Human
        (targeted therapeutic delivery of vitamin D compds.)
TT
     Vitamin D receptors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (targeted therapeutic delivery of vitamin D compds.)
\mathbf{IT}
     Antibodies and Immunoglobulins
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (targeted therapeutic delivery of vitamin D compds.)
IT
     107-30-2, Chloromethyl methyl ether
                                            70550-73-1 211865-86-0
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (targeted therapeutic delivery of vitamin D compds.)
IT
     81522-68-1P 140710-96-9P 144034-23-1P
     211865-87-1P 211865-88-2P 211865-89-3P
     211865-90-6P 211865-92-8P 211865-93-9P
     211865-94-0P 211865-96-2P 211865-97-3P
     211865-98-4P 211865-99-5P 211866-01-2P
     211866-02-3P 211866-03-4P 211866-04-5P
     211866-06-7P 211866-07-8P 211866-08-9P
     211866-09-0P 211866-11-4P 211866-12-5P
     211866-13-6P 211866-15-8P 211866-16-9P
     211866-17-0P 211866-19-2P 557072-52-3P
     557072-53-4P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (targeted therapeutic delivery of vitamin D compds.)
IT
     211865-95-1P
     RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent);
     USES (Uses)
        (targeted therapeutic delivery of vitamin D compds.)
TT
     211866-10-3P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (targeted therapeutic delivery of vitamin D compds.)
IT
     211865-91-7P 211866-00-1P 211866-05-6P
     211866-14-7P 211866-18-1P 557072-54-5P
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (targeted therapeutic delivery of vitamin D compds.)
     1406-16-2D, Vitamin d, conjugates
                                                      10596-23-3
IT
                                          2809-21-4
     32222-06-3, 1\alpha,25-Dihydroxyvitamin D3
                                             40391-99-9
     41294-56-8, 1\alpha-Hydroxyvitamin D3 54573-75-0,
     1\alpha-Hydroxyvitamin D2 60133-18-8, 1\alpha, 25-
     Dihydroxyvitamin D2 66376-36-1, Alendronate
                                   89987-06-4, Tiludronate
     83805-11-2, Falecalcitriol
     103909-75-7, Maxacalcitol 105462-24-6
     112965-21-6, Calcipotriol 114084-78-5,
     Ibandronate 118072-93-8, Zoledronate
     124043-51-2, 1\alpha, 24-Dihydroxyvitamin D2 131249-38-2
      1\alpha, 25-Dihydroxyvitamin D4 131918-61-1, Paricalcitol
     134404-52-7, Seocalcitol 157893-62-4,
     1\alpha, 24-Dihydroxyvitamin D4
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (targeted therapeutic delivery of vitamin D compds.)
     211865-86-0
IT
```

Absolute stereochemistry.

Double bond geometry as shown.

Absolute stereochemistry.

Double bond geometry as shown.

RN 144034-23-1 HCAPLUS
CN Phosphonic acid, (4-aminobutylidene)bis-, tetrakis(1-methylethyl) ester
(9CI) (CA INDEX NAME)

RN 211865-87-1 HCAPLUS

CN 9,10-Secoergosta-5,7,10(19),22-tetraen-24-ol, 1,3-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-, carbonochloridate, $(1\alpha,3\beta,5E,7E,22E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

RN 211865-88-2 HCAPLUS

On 9,10-Secoergosta-5,7,10(19),22-tetraen-24-ol, 1,3-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-, [4,4-bis[bis(1-methylethoxy)phosphinyl]butyl]carbamate, (1α,3β,5E,7E,22E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

PAGE 1-A

PAGE 1-B

RN 211865-89-3 HCAPLUS

CN 9,10-Secoergosta-5,7,10(19),22-tetraene-1,3,24-triol, 24-[[4,4-bis[bis(1-methylethoxy)phosphinyl]butyl]carbamate], (1α,3β,5E,7E,22E)(9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

PAGE 1-A

PAGE 1-B

-- OPr-i

RN 211865-90-6 HCAPLUS

CN 9,10-Secoergosta-5,7,10(19),22-tetraene-1,3,24-triol, 24-[(4,4-diphosphonobutyl)carbamate] (9CI) (CA INDEX NAME)

RN 211865-92-8 HCAPLUS CN Silane, [[(1α , 3β , 5E, 7E, 22E) -24-(methoxymethoxy)-9,10-secoergosta-5,7,10(19),22-tetraene-1,3-diyl]bis(oxy)]bis[(1,1-dimethylethyl)dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 211865-93-9 HCAPLUS CN 9,10-Secoergosta-5,7,10(19),22-tetraene-1,3-diol, 24-(methoxymethoxy)-, $(1\alpha,3\beta,5E,7E,22E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

RN 211865-94-0 HCAPLUS 9,10-Secoergosta-5,7,10(19),22-tetraen-1-ol, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-24-(methoxymethoxy)-, $(1\alpha,3\beta,5E,7E,22E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 211865-96-2 HCAPLUS

CN 9,10-Secoergosta-5,7,10(19),22-tetraen-1-ol, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-24-(methoxymethoxy)-, carbonochloridate, $(1\alpha,3\beta,5E,7E,22E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 211865-97-3 HCAPLUS

CN 9,10-Secoergosta-5,7,10(19),22-tetraen-1-ol, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-24-(methoxymethoxy)-, [4,4-bis[bis(1-methylethoxy)phosphinyl]butyl]carbamate, $(1\alpha,3\beta,5E,7E,22E)$ - (9CI) (CA INDEX NAME)

PAGE 1-B

RN 211865-98-4 HCAPLUS CN 9,10-Secoergosta-5,7,10(19),22-tetraene-1,3-diol, 24-(methoxymethoxy)-, 1-[[4,4-bis[bis(1-methylethoxy)phosphinyl]butyl]carbamate], $(1\alpha,3\beta,5E,7E,22E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

PAGE 1-A

PAGE 1-B

RN 211865-99-5 HCAPLUS

CN 9,10-Secoergosta-5,7,10(19),22-tetraene-1,3,24-triol, 1-[(4,4-diphosphonobutyl)carbamate], (1α,3β,5E,7E,22E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

PAGE 1-A

$$H_2O_3P$$
 CH_2
 H_2O_3P
 $H_2O_$

PAGE 1-B

Pr-i

RN 211866-01-2 HCAPLUS

CN 9,10-Secoergosta-5,7,10(19),22-tetraen-3-ol, 1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-24-(methoxymethoxy)-, carbonochloridate, $(1\alpha,3\beta,5E,7E,22E)$ - (9CI) (CA INDEX NAME)

RN 211866-02-3 HCAPLUS

CN 9,10-Secoergosta-5,7,10(19),22-tetraen-3-ol, 1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-24-(methoxymethoxy)-,
[4,4-bis[bis(1-methylethoxy)phosphinyl]butyl]carbamate,
(1α,3β,5E,7E,22E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

PAGE 1-A

PAGE 1-B

OMe

RN 211866-03-4 HCAPLUS

9,10-Secoergosta-5,7,10(19),22-tetraene-1,3-diol, 24-(methoxymethoxy)-,
3-[[4,4-bis[bis(1-methylethoxy)phosphinyl]butyl]carbamate],
(1α,3β,5E,7E,22E)- (9CI) (CA INDEX NAME)

PAGE 1-B

_OMe

RN 211866-04-5 HCAPLUS

CN 9,10-Secoergosta-5,7,10(19),22-tetraene-1,3,24-triol, 3-[(4,4-diphosphonobuty1)carbamate], $(1\alpha,3\beta,5E,7E,22E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

$$H_{2}O_{3}P$$
 CH_{2}
 $H_{2}O_{3}P$
 CH_{2}
 $H_{2}O_{3}P$
 $H_{3}O_{3}P$
 $H_{4}O_{5}P$
 $H_{5}O_{6}P$
 $H_{5}O_{6}P$
 $H_{6}O_{6}P$
 $H_{7}O_{7}P$
 $H_{7}O_{7}$

RN 211866-07-8 HCAPLUS

CN Silane, [[$(1\alpha, 3\beta, 5Z, 7E) - 25 - [(tetrahydro - 2H - pyran - 2 - yl) oxy] - 9, 10 - secocholesta - 5, 7, 10 (19) - triene - 1, 3 - diyl]bis (oxy)]bis[(1, 1 - dimethylethyl)dimethyl - (9CI) (CA INDEX NAME)$

RN 211866-08-9 HCAPLUS CN 9,10-Secocholesta-5,7,10(19)-triene-1,3-diol, 25-[(tetrahydro-2H-pyran-2-yl)oxy]-, (1α,3β,5Z,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 211866-09-0 HCAPLUS CN 9,10-Secocholesta-5,7,10(19)-trien-1-ol, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-25-[(tetrahydro-2H-pyran-2-yl)oxy]-, $(1\alpha,3\beta,5Z,7E)$ - (9CI) (CA INDEX NAME)

RN 211866-11-4 HCAPLUS
CN 9,10-Secocholesta-5,7,10(19)-trien-1-ol, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-25-[(tetrahydro-2H-pyran-2-yl)oxy]-,

carbonochloridate, $(1\alpha, 3\beta, 5Z, 7E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 211866-12-5 HCAPLUS CN 9,10-Secocholesta-5,7,10(19)-trien-1-ol, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-25-[(tetrahydro-2H-pyran-2-yl)oxy]-, [4,4-bis[bis(1-methylethoxy)phosphinyl]butyl]carbamate, $(1\alpha,3\beta,5Z,7E)$ - (9CI) (CA INDEX NAME)

PAGE 1-B

RN 211866-13-6 HCAPLUS

CN 9,10-Secocholesta-5,7,10(19)-triene-1,3-diol, 25-[(tetrahydro-2H-pyran-2-yl)oxy]-, 1-[[4,4-bis[bis(1-methylethoxy)phosphinyl]butyl]carbamate], $(1\alpha,3\beta,5Z,7E)$ - (9CI) (CA INDEX NAME)

PAGE 1-B

RN 211866-15-8 HCAPLUS

CN 9,10-Secocholesta-5,7,10(19)-trien-3-ol, 1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-25-[(tetrahydro-2H-pyran-2-yl)oxy]-, carbonochloridate, (1α,3β,5Z,7E)- (9CI) (CA INDEX NAME)

RN 211866-16-9 HCAPLUS
CN 9,10-Secocholesta-5,7,10(19)-trien-3-ol, 1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-25-[(tetrahydro-2H-pyran-2-yl)oxy]-,
 [4,4-bis[bis(1-methylethoxy)phosphinyl]butyl]carbamate,
 (1α,3β,5Z,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 211866-17-0 HCAPLUS CN 9,10-Secocholesta-5,7,10(19)-triene-1,3-diol, 25-[(tetrahydro-2H-pyran-2-yl)oxy]-, 3-[[4,4-bis[bis(1-methylethoxy)phosphinyl]butyl]carbamate], $(1\alpha,3\beta,5Z,7E)- (9CI) \quad (CA \; INDEX \; NAME)$

RN 211866-19-2 HCAPLUS

CN 9,10-Secocholesta-5,7,10(19)-trien-25-ol, 1,3-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-, carbonochloridate, $(1\alpha,3\beta,5Z,7E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 557072-52-3 HCAPLUS

CN 9,10-Secocholesta-5,7,10(19)-trien-25-ol, 1,3-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-, [4,4-bis[bis(1-methylethoxy)phosphinyl]butyl]carbamate, $(1\alpha,3\beta,5Z,7E)$ - (9CI) (CA INDEX NAME)

PAGE 1-B

RN 557072-53-4 HCAPLUS

CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 25-[[4,4-bis[bis(1-methylethoxy)phosphinyl]butyl]carbamate], $(1\alpha,3\beta,5Z,7E)$ - (9CI) (CA INDEX NAME)

PAGE 1-B

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OPr-i
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∕oPr-i

IT 211865-95-1P

RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(targeted therapeutic delivery of vitamin D compds.)

RN 211865-95-1 HCAPLUS

CN 9,10-Secoergosta-5,7,10(19),22-tetraen-3-ol, 1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-24-(methoxymethoxy)-, $(1\alpha,3\beta,5E,7E,22E)$ - (9CI) (CA INDEX NAME)

IT 211866-10-3P

RL: SPN (Synthetic preparation); PREP (Preparation) (targeted therapeutic delivery of vitamin D compds.)

RN 211866-10-3 HCAPLUS

CN 9,10-Secocholesta-5,7,10(19)-trien-3-ol, 1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-25-[(tetrahydro-2H-pyran-2-yl)oxy]-, $(1\alpha,3\beta,5Z,7E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 211866-00-1 HCAPLUS

CN 9,10-Secoergosta-5,7,10(19),22-tetraene-1,3,24-triol, 1-[(4,4-diphosphonobutyl)carbamate], $(1\alpha,3\beta,5Z,7E,22E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

PAGE 1-B

RN 211866-05-6 HCAPLUS

CN 9,10-Secoergosta-5,7,10(19),22-tetraene-1,3,24-triol, 3-[(4,4-diphosphonobutyl)carbamate], $(1\alpha,3\beta,5Z,7E,22E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

HO
$$\frac{(CH_2)_3}{PO_3H_2}$$
 $\frac{PO_3H_2}{R}$
 $\frac{E}{Me}$
 $\frac{H}{Me}$
 $\frac{R}{Me}$
 $\frac{R}{Me}$
 $\frac{R}{Me}$
 $\frac{R}{Me}$
 $\frac{R}{Me}$
 $\frac{R}{Me}$
 $\frac{R}{Me}$
 $\frac{R}{Me}$
 $\frac{R}{Me}$

RN 211866-14-7 HCAPLUS

CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 1-[(4,4-diphosphonobutyl)carbamate], $(1\alpha,3\beta,5Z,7E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

PAGE 1-A

PAGE 1-B

Me Me

RN 211866-18-1 HCAPLUS

CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 3-[(4,4-diphosphonobutyl)carbamate], $(1\alpha,3\beta,5Z,7E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

HO R
$$(CH_2)_3$$
 PO_3H_2 PO_3H_2

RN 557072-54-5 HCAPLUS

CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 25-[(4,4-diphosphonobutyl)carbamate], (1α,3β,5Z,7E)- (9CI) (CA INDEX NAME)

PAGE 1-B

-- PO3H2

```
32222-06-3, 1\alpha, 25-Dihydroxyvitamin D3 40391-99-9 41294-56-8, 1\alpha-Hydroxyvitamin D3 54573-75-0, 1\alpha-Hydroxyvitamin D2 60133-18-8, 1\alpha, 25-
IT
      Dihydroxyvitamin D2 66376-36-1, Alendronate
      83805-11-2, Falecalcitriol 103909-75-7, Maxacalcitol
      105462-24-6 112965-21-6, Calcipotriol
      114084-78-5, Ibandronate 118072-93-8, Zoledronate 124043-51-2, 1α,24-Dihydroxyvitamin D2
      131249-38-2, 1\alpha, 25-Dihydroxyvitamin D4 131918-61-1
      , Paricalcitol 134404-52-7, Seocalcitol 157893-62-4,
      1\alpha, 24-Dihydroxyvitamin D4
      RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
          (targeted therapeutic delivery of vitamin D compds.)
RN
      32222-06-3 HCAPLUS
      9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, (1\alpha,3\beta,5Z,7E)-
CN
       (9CI)
               (CA INDEX NAME)
```

Absolute stereochemistry. Rotation (+). Double bond geometry as shown.

OH

R

S

$$CH_2$$

E

H

R

R

 $(CH_2)_3$

Me

Me

HO

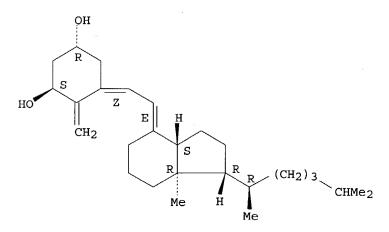
Me

RN 40391-99-9 HCAPLUS CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{OH} \\ | \\ \text{H}_2\text{O}_3\text{P} - \text{C} - \text{CH}_2 - \text{CH}_2 - \text{NH}_2 \\ | \\ \text{PO}_3\text{H}_2 \end{array}$$

RN 41294-56-8 HCAPLUS CN 9,10-Secocholesta-5,7,10(19)-triene-1,3-diol, $(1\alpha,3\beta,5Z,7E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+). Double bond geometry as shown.



RN 54573-75-0 HCAPLUS CN 9,10-Secoergosta-5,7,10(19),22-tetraene-1,3-diol, $(1\alpha,3\beta,5Z,7E,22E)$ - (9CI) (CA INDEX NAME)

RN 60133-18-8 HCAPLUS CN 9,10-Secoergosta-5,7,10(19),22-tetraene-1,3,25-triol, $(1\alpha,3\beta,5Z,7E,22E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 66376-36-1 HCAPLUS CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{OH} \\ | \\ \text{H}_2\text{O}_3\text{P} - \text{C} - (\text{CH}_2)_3 - \text{NH}_2 \\ | \\ \text{PO}_3\text{H}_2 \end{array}$$

RN 83805-11-2 HCAPLUS
CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 26,26,26,27,27,27-hexafluoro-, (1α,3β,5Ζ,7Ε)- (9CI) (CA INDEX NAME)

RN 103909-75-7 HCAPLUS

CN 1,3-Cyclohexanediol, 4-methylene-5-[(2E)-[(1S,3aS,7aS)-octahydro-1-[(1S)-1-(3-hydroxy-3-methylbutoxy)ethyl]-7a-methyl-4H-inden-4-ylidene]ethylidene]-, (1R,3S,5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 105462-24-6 HCAPLUS

CN Phosphonic acid, [1-hydroxy-2-(3-pyridinyl)ethylidene]bis-(9CI) (CA INDEX NAME)

RN 112965-21-6 HCAPLUS

CN 9,10-Secochola-5,7,10(19),22-tetraene-1,3,24-triol, 24-cyclopropyl-, $(1\alpha,3\beta,5Z,7E,22E,24S)$ - (9CI) (CA INDEX NAME)

RN 114084-78-5 HCAPLUS
CN Phosphonic acid, [1-hydroxy-3-(methylpentylamino)propylidene]bis- (9CI)
(CA INDEX NAME)

RN 118072-93-8 HCAPLUS

CN Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis- (9CI) (CA INDEX NAME)

RN 124043-51-2 HCAPLUS

Absolute stereochemistry.

Double bond geometry as shown.

RN 131249-38-2 HCAPLUS CN 9,10-Secoergosta-5,7,10(19)-triene-1,3,25-triol, (1α,3β,5Z,7E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 131918-61-1 HCAPLUS CN 19-Nor-9,10-secoergosta-5,7,22-triene-1,3,25-triol, $(1\alpha,3\beta,7E,22E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 134404-52-7 HCAPLUS
CN 1,3-Cyclohexanediol, 5-[(2E)-[(1R,3aS,7aR)-1-[(1R,2E,4E)-6-ethyl-6-hydroxy-1-methyl-2,4-octadienyl]octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-

4-methylene-, (1R,3S,5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 157893-62-4 HCAPLUS CN 9,10-Secoergosta-5,7,10(19)-triene-1,3,24-triol, (1α,3β,5Z,7E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

L30 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:696655 HCAPLUS

DN 137:210938

ED Entered STN: 13 Sep 2002

TI Treatment of hyperproliferative diseases using active vitamin D analogues

IN Mazess, Richard B.

PA Bone Care International, Inc., USA

SO U.S. Pat. Appl. Publ., 15 pp., Cont.-in-part of U.S. Ser. No. 891,814. CODEN: USXXCO

DT Patent

LA English

IC ICM A61K031-59

NCL 514167000

CC 1-6 (Pharmacology)

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		US 2002025950	A1	20020228	US 2001-891814	20010626 <
		US 6503893	B2	20030107		
		WO 2003045333	A2	20030605	WO 2002-US38263	20021126
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os
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AB
     The present invention provides a method of inhibiting the
     hyperproliferative cellular activity of neoplasms and other
     hyperproliferative diseases with an active vitamin D compound utilizing a
     high dose, episodic treatment protocol. Patients with advanced
     androgen-independent prostate cancer were treated i.v. with
     1\alpha, 24-dihydroxyvitamin D2.
ST
     hyperproliferative disease treatment vitamin D analog; prostate cancer
     treatment dihydroxyvitamin D2 intravenous
IT
     Prostate gland, neoplasm
        (adenocarcinoma, metastasis; treatment of hyperproliferative diseases
        using active vitamin D analogs)
TΤ
     Prostate gland, neoplasm
        (adenocarcinoma; treatment of hyperproliferative diseases using active
        vitamin D analogs)
TT
     Bone, disease
        (agent treating; treatment of hyperproliferative diseases using active
        vitamin D analogs)
IT
     Microtubule
        (agents inhibiting; treatment of hyperproliferative diseases using
        active vitamin D analogs)
IT
        (agents; treatment of hyperproliferative diseases using active vitamin
        D analogs)
IT
     Antitumor agents
        (antibiotic; treatment of hyperproliferative diseases using active
        vitamin D analogs)
ΙT
    Nutrients
        (antinutrients; treatment of hyperproliferative diseases using active
        vitamin D analogs)
IT
    Antibiotics
        (antitumor; treatment of hyperproliferative diseases using active
```

vitamin D analogs)

ΙT Anthracyclines RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (antitumor; treatment of hyperproliferative diseases using active vitamin D analogs) ITVitamin D receptors RL: BSU (Biological study, unclassified); BIOL (Biological study) (cells expressing; treatment of hyperproliferative diseases using active vitamin D analogs) ITUterus, neoplasm (cervix; treatment of hyperproliferative diseases using active vitamin D analogs) IT Intestine, neoplasm (colon; treatment of hyperproliferative diseases using active vitamin D analogs) ITUterus, neoplasm (endometrium; treatment of hyperproliferative diseases using active vitamin D analogs) ITCell proliferation Disease, animal (hyperproliferative; treatment of hyperproliferative diseases using active vitamin D analogs) IT Cell differentiation (inducers; treatment of hyperproliferative diseases using active vitamin D analogs) IT Drug delivery systems (injections, i.v.; treatment of hyperproliferative diseases using active vitamin D analogs) IT Leukemia (lymphocytic; treatment of hyperproliferative diseases using active vitamin D analogs) IT Thyroid gland, neoplasm (medullary carcinoma; treatment of hyperproliferative diseases using active vitamin D analogs) IT Leukemia (myelogenous; treatment of hyperproliferative diseases using active vitamin D analogs) ITNeck, anatomical (neoplasm; treatment of hyperproliferative diseases using active vitamin D analogs) IT Drug delivery systems (oral; treatment of hyperproliferative diseases using active vitamin D analogs) Bone, neoplasm IT (osteosarcoma; treatment of hyperproliferative diseases using active vitamin D analogs) Drug delivery systems IT (parenterals; treatment of hyperproliferative diseases using active vitamin D analogs) ΙT Eye, neoplasm (retinoblastoma; treatment of hyperproliferative diseases using active vitamin D analogs) IT Animal tissue, disease (soft, neoplasm, sarcoma; treatment of hyperproliferative diseases using active vitamin D analogs) IT Carcinoma (squamous cell; treatment of hyperproliferative diseases using active vitamin D analogs) IT Alkylating agents, biological Antitumor agents Bladder, neoplasm

Cytotoxic agents Drug delivery systems

```
Head, neoplasm
     Human
     Liver, neoplasm
     Lung, neoplasm
     Lymphoma
     Mammary gland, neoplasm
     Melanoma
     Multiple myeloma
     Neoplasm
     Ovary, neoplasm
     Pancreas, neoplasm
     Prostate gland, neoplasm
     Psoriasis
     Sarcoma
     Testis, neoplasm
        (treatment of hyperproliferative diseases using active vitamin D
        analogs)
IT
     13598-36-2D, Phosphonic acid, alkylidenebis-derivs., compds.
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (Bisphosphonate, antihypercalcemic agents; treatment of
        hyperproliferative diseases using active vitamin D analogs)
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     1406-16-2D, Vitamin D, analogs or compds.
     RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
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        (active hypocalcemic; treatment of hyperproliferative diseases using
        active vitamin D analogs)
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     33069-62-4, Paclitaxel 40391-99-9
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     (Biological study); USES (Uses)
        (coadministration of active vitamin D and; treatment of
        hyperproliferative diseases using active vitamin D analogs)
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     7440-70-2, Calcium, biological studies
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        (hypercalcemia, reduced risk of; treatment of hyperproliferative
        diseases using active vitamin D analogs)
IT
     80449-01-0, Topoisomerase
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        vitamin D analogs)
ΙT
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     7440-06-4D, Platinum, compds. 32222-06-3, 1\alpha, 25-
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     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (treatment of hyperproliferative diseases using active vitamin D
        analogs)
IT
     40391-99-9
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
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(coadministration of active vitamin D and; treatment of hyperproliferative diseases using active vitamin D analogs)
40391-99-9 HCAPLUS

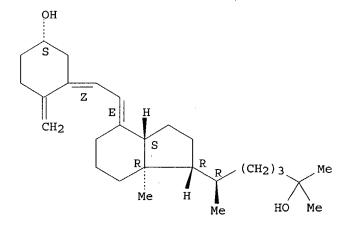
CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{OH} \\ | \\ \text{H}_2\text{O}_3\text{P} - \begin{array}{c} \text{C} - \text{CH}_2 - \text{CH}_2 - \text{NH}_2 \\ | \\ \text{PO}_3\text{H}_2 \end{array}$$

RN

CN 9,10-Secocholesta-5,7,10(19)-triene-3,25-diol, (3 β ,5Z,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.



RN 124043-51-2 HCAPLUS CN 9,10-Secoergosta-5,7,10(19),22-tetraene-1,3,24-triol, $(1\alpha,3\beta,5Z,7E,22E,24\xi)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 156316-85-7 HCAPLUS CN 9,10-Secoergosta-5,7,10(19),22-tetraene-1,3,24-triol, $(1\alpha,3\beta,5Z,7E,22E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

RN 156316-86-8 HCAPLUS CN 9,10-Secoergosta-5,7,10(19),22-tetraene-1,3,24-triol, $(1\alpha,3\beta,5Z,7E,22E,24R)$ - (9CI) (CA INDEX NAME) Absolute stereochemistry.

Double bond geometry as shown.

RN 157893-62-4 HCAPLUS CN 9,10-Secoergosta-5,7,10(19)-triene-1,3,24-triol, (1α,3β,5Z,7E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

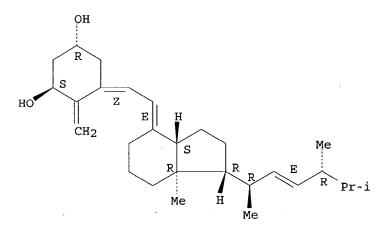
Double bond geometry as shown.

Absolute stereochemistry. Rotation (+). Double bond geometry as shown.

 $\begin{array}{lll} \text{RN} & 54573-75-0 & \text{HCAPLUS} \\ \text{CN} & 9,10\text{-Secoergosta-5,7,10(19),22-tetraene-1,3-diol,} \\ & & (1\alpha,3\beta,5Z,7E,22E)\text{- (9CI)} & (\text{CA INDEX NAME}) \end{array}$

Absolute stereochemistry.

Double bond geometry as shown.



RN 58050-56-9 HCAPLUS CN 9,10-Secoergosta-5,7,10(19),22-tetraene-3,24-diol, $(3\beta,5Z,7E,22E,24\xi)$ - (9CI) (CA INDEX NAME)

RN 60133-18-8 HCAPLUS CN 9,10-Secoergosta-5,7,10(19),22-tetraene-1,3,25-triol, $(1\alpha,3\beta,5Z,7E,22E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 143032-85-3 HCAPLUS CN 9,10-Secoergosta-5,7,10(19)-triene-1,3-diol, $(1\alpha,3\beta,5Z,7E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

RN 186489-58-7 HCAPLUS CN 9,10-Secoergosta-5,7,10(19)-triene-1,3,24,25-tetrol, $(1\alpha,3\beta,5Z,7E,24\xi)$ - (9CI) (CA INDEX NAME) Absolute stereochemistry.

Double bond geometry as shown.

RN 254448-88-9 HCAPLUS. CN 9,10-Secoergosta-5,7,10(19)-diene-3,24-diol, (3β,5Z,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 457048-34-9 HCAPLUS CN $9,10-Secoergosta-5,7,10(19),22-tetraene-1,3,24,25-tetrol, <math>(1\alpha,3\beta,5Z,7E,22E,25\xi)-(9CI)$ (CA INDEX NAME)

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L30 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN
AN
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ED
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TI
     Targeted therapeutic delivery of vitamin D compounds
IN
     Mazess, Richard B.; Bishop, Charles W.
PA
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SO
     PCT Int. Appl., 55 pp.
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     The present invention is directed to a conjugate which includes at least
     one vitamin D moiety thereof and at least one targeting mol. moiety to
     pharmaceutical compns. of the conjugate, and to methods for using the
     conjugate for target-specific delivery of vitamin D or analogs thereof to
     tissues in need thereof. When a particularly preferred form is
     administered to a patient, the targeting mol. component of the conjugate
     of this invention seeks out and binds to a tissue of interest, such as
     bone or tumor tissue, where the vitamin D has a therapeutic effect. A
     conjugate of 1\alpha, 24-dihydroxyvitamin D2 and aminoalkyl
     1,1-bisphosphonate linked at C-24 of the vitamin D moiety was prepared
     drug targeting vitamin D2 bisphosphonate conjugate
ST
IT
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     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (antiestrogens; vitamin D2 conjugates for targeted delivery)
IT
     Estrogens
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (conjugated; vitamin D2 conjugates for targeted delivery)
IT
     Drug delivery systems
        (enteric-coated; vitamin D2 conjugates for targeted delivery)
IT
     Drug delivery systems
        (oral; vitamin D2 conjugates for targeted delivery)
IT
     Toxins
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (pertussis; vitamin D2 conjugates for targeted delivery)
IT
     Bone, disease
        (treatment of; vitamin D2 conjugates for targeted delivery)
TΤ
     Antitumor agents
     Cytotoxic agents
     Drug targeting
        (vitamin D2 conjugates for targeted delivery)
TΤ
     Bone morphogenetic proteins
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (vitamin D2 conjugates for targeted delivery)
TT
     Transforming growth factors
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (\beta-; vitamin D2 conjugates for targeted delivery)
IT
                        107-30-2, Chloromethyl methyl ether
     75-44-5, Phosgene
                                                                18162-48-6,
     tert-Butyldimethylsilyl chloride
                                        70550-73-1
                                                      81522-68-1
     144034-23-1 211865-86-0
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (preparation of vitamin D2 analog-bisphosphonate conjugates for targeted
        delivery)
IT
     140710-96-9P 211865-87-1P 211865-88-2P
     211865-89-3P 211865-90-6P 211865-92-8P
     211865-93-9P 211865-94-0P 211865-95-1P
     211865-96-2P 211865-97-3P 211865-98-4P
     211865-99-5P 211866-01-2P 211866-02-3P
     211866-03-4P 211866-04-5P
                                 211866-06-7P
     211866-07-8P 211866-08-9P 211866-09-0P
     211866-10-3P 211866-11-4P 211866-12-5P
     211866-13-6P 211866-15-8P 211866-16-9P
     211866-17-0P 211866-19-2P 211866-20-5P
     211866-21-6P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation of vitamin D2 analog-bisphosphonate conjugates for targeted
        delivery)
IT
     211865-91-7P 211866-00-1P 211866-05-6P
     211866-14-7P 211866-18-1P 211866-22-7P
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
```

(preparation of vitamin D2 analog-bisphosphonate conjugates for targeted delivery)

IT 51-21-8, 5-Fluorouracil 53-43-0, Dehydroepiandrosterone 59-05-2, Methotrexate 60-54-8, Tetracycline 127-07-1, Hydroxyurea 148-82-3, Melphalan 1404-00-8, Mitomycin 7440-42-8, Boron, biological studies 9007-12-9, Calcitonin 13408-78-1, Cobalamin 15663-27-1, Cisplatin 20830-81-3, Daunomycin 25316-40-9, Adriamycin 29069-24-7, Prednimustine 58957-92-9, Idarubicin 62899-40-5, Estromustine 114949-22-3, Activin

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (vitamin D2 conjugates for targeted delivery)

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD RE

- (1) Bouillon, R; US 5232836 A 1993 HCAPLUS
- (2) Isis Pharmaceuticals Inc; WO 9307883 A 1993 HCAPLUS
- (3) Londowski, J; J PHARMACOL EXP THER 1986, V237(3), P837 HCAPLUS
- (4) Peterson, A; US 5691328 A 1997 HCAPLUS
- IT 144034-23-1 211865-86-0

RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of vitamin D2 analog-bisphosphonate conjugates for targeted
 delivery)

RN 144034-23-1 HCAPLUS

CN Phosphonic acid, (4-aminobutylidene)bis-, tetrakis(1-methylethyl) ester. (9CI) (CA INDEX NAME)

RN 211865-86-0 HCAPLUS

CN 9,10-Secoergosta-5,7,10(19),22-tetraen-24-ol, 1,3-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-, $(1\alpha,3\beta,5E,7E,22E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

IT 140710-96-9P 211865-87-1P 211865-88-2P 211865-89-3P 211865-90-6P 211865-92-8P 211865-93-9P 211865-94-0P 211865-95-1P 211865-96-2P 211865-97-3P 211865-98-4P

211865-99-5P 211866-01-2P 211866-02-3P 211866-03-4P 211866-04-5P 211866-07-8P 211866-08-9P 211866-09-0P 211866-10-3P 211866-11-4P 211866-12-5P 211866-13-6P 211866-15-8P 211866-16-9P 211866-17-0P 211866-19-2P 211866-20-5P 211866-21-6P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation of vitamin D2 analog-bisphosphonate conjugates for targeted delivery) RN140710-96-9 HCAPLUS 9,10-Secocholesta-5,7,10(19)-trien-25-ol, 1,3-bis[[(1,1-CNdimethylethyl)dimethylsilyl]oxy]-, $(1\alpha, 3\beta, 5Z, 7E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

RN 211865-87-1 HCAPLUS CN 9,10-Secoergosta-5,7,10(19),22-tetraen-24-ol, 1,3-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-, carbonochloridate, $(1\alpha,3\beta,5E,7E,22E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

RN 211865-88-2 HCAPLUS 9,10-Secoergosta-5,7,10(19),22-tetraen-24-ol, 1,3-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-, [4,4-bis[bis(1-methylethoxy)phosphinyl]butyl]carbamate, $(1\alpha,3\beta,5E,7E,22E)$ - (9CI) (CA INDEX NAME)

PAGE 1-B

RN 211865-89-3 HCAPLUS

CN 9,10-Secoergosta-5,7,10(19),22-tetraene-1,3,24-triol, 24-[[4,4-bis[bis(1-methylethoxy)phosphinyl]butyl]carbamate], $(1\alpha,3\beta,5E,7E,22E)$ -(9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

PAGE 1-A

PAGE 1-B

-- OPr-i

OPr-i

RN 211865-90-6 HCAPLUS

CN 9,10-Secoergosta-5,7,10(19),22-tetraene-1,3,24-triol, 24-[(4,4-diphosphonobutyl)carbamate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 211865-92-8 HCAPLUS

CN Silane, [[(1α ,3 β ,5E,7E,22E)-24-(methoxymethoxy)-9,10-secoergosta-5,7,10(19),22-tetraene-1,3-diyl]bis(oxy)]bis[(1,1-dimethylethyl)dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 211865-93-9 HCAPLUS

CN 9,10-Secoergosta-5,7,10(19),22-tetraene-1,3-diol, 24-(methoxymethoxy)-, (1α,3β,5E,7E,22E)- (9CI) (CA INDEX NAME)

RN 211865-94-0 HCAPLUS

CN 9,10-Secoergosta-5,7,10(19),22-tetraen-1-ol, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-24-(methoxymethoxy)-, $(1\alpha,3\beta,5E,7E,22E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 211865-95-1 HCAPLUS

CN 9,10-Secoergosta-5,7,10(19),22-tetraen-3-ol, 1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-24-(methoxymethoxy)-, $(1\alpha,3\beta,5E,7E,22E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 211865-96-2 HCAPLUS

CN 9,10-Secoergosta-5,7,10(19),22-tetraen-1-ol, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-24-(methoxymethoxy)-, carbonochloridate, (1α,3β,5E,7E,22E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

RN 211865-97-3 HCAPLUS

CN 9,10-Secoergosta-5,7,10(19),22-tetraen-1-ol, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-24-(methoxymethoxy)-, [4,4-bis[bis(1-methylethoxy)phosphinyl]butyl]carbamate, $(1\alpha,3\beta,5E,7E,22E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

PAGE 1-A

PAGE 1-B

CN9,10-Secoergosta-5,7,10(19),22-tetraene-1,3-diol, 24-(methoxymethoxy)-, 1-[[4,4-bis[bis(1-methylethoxy)phosphinyl]butyl]carbamate], $(1\alpha, 3\beta, 5E, 7E, 22E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

PAGE 1-A

PAGE 1-B

211865-99-5 HCAPLUS RNCN

9,10-Secoergosta-5,7,10(19),22-tetraene-1,3,24-triol, 1-[(4,4-diphosphonobuty1)carbamate], (1 α ,3 β ,5E,7E,22E)- (9CI) (CA INDEX NAME)

$$H_{2}O_{3}P$$
 $(CH_{2})_{3}$
 $H_{1}O_{2}$
 $(CH_{2})_{3}$
 $H_{2}O_{3}P$
 $(CH_{2})_{3}$
 $H_{2}O_{3}P$
 $(CH_{2})_{3}$
 $(CH_{2})_$

PAGE 1-B

∕Pr-i

RN 211866-01-2 HCAPLUS CN 9,10-Secoergosta-5,7,10(19),22-tetraen-3-ol, 1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-24-(methoxymethoxy)-, carbonochloridate, $(1\alpha,3\beta,5E,7E,22E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 211866-02-3 HCAPLUS CN 9,10-Secoergosta-5,7,10(19),22-tetraen-3-ol, 1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-24-(methoxymethoxy)-, [4,4-bis[bis(1-methylethoxy)phosphinyl]butyl]carbamate, $(1\alpha,3\beta,5E,7E,22E)$ - (9CI) (CA INDEX NAME)

PAGE 1-B

OMe

RN 211866-03-4 HCAPLUS

CN 9,10-Secoergosta-5,7,10(19),22-tetraene-1,3-diol, 24-(methoxymethoxy)-, 3-[[4,4-bis[bis(1-methylethoxy)phosphinyl]butyl]carbamate], $(1\alpha,3\beta,5E,7E,22E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

PAGE 1-A

PAGE 1-B

_OMe

RN 211866-04-5 HCAPLUS

CN 9,10-Secoergosta-5,7,10(19),22-tetraene-1,3,24-triol, 3-[(4,4-diphosphonobutyl)carbamate], $(1\alpha,3\beta,5E,7E,22E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

H2O3P (CH2) 3 HO Me H Me H Me
$$^{\text{R}}$$
 $^{\text{R}}$ $^{\text{$

RN 211866-07-8 HCAPLUS

CN Silane, [[$(1\alpha, 3\beta, 5Z, 7E) - 25 - [(tetrahydro - 2H - pyran - 2 - yl) oxy] - 9, 10 - secocholesta - 5, 7, 10 (19) - triene - 1, 3 - diyl]bis (oxy)]bis[(1, 1 - dimethylethyl)dimethyl - (9CI) (CA INDEX NAME)$

RN 211866-08-9 HCAPLUS CN 9,10-Secocholesta-5,7,10(19)-triene-1,3-diol, 25-[(tetrahydro-2H-pyran-2-yl)oxy]-, (1α,3β,5Z,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 211866-09-0 HCAPLUS

CN 9,10-Secocholesta-5,7,10(19)-trien-1-ol, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-25-[(tetrahydro-2H-pyran-2-yl)oxy]-, $(1\alpha,3\beta,5Z,7E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 211866-10-3 HCAPLUS

CN 9,10-Secocholesta-5,7,10(19)-trien-3-ol, 1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-25-[(tetrahydro-2H-pyran-2-yl)oxy]-, $(1\alpha,3\beta,5Z,7E)$ - (9CI) (CA INDEX NAME)

RN 211866-11-4 HCAPLUS

CN 9,10-Secocholesta-5,7,10(19)-trien-1-ol, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-25-[(tetrahydro-2H-pyran-2-yl)oxy]-, carbonochloridate, (1α,3β,5Z,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 211866-12-5 HCAPLUS

9,10-Secocholesta-5,7,10(19)-trien-1-ol, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-25-[(tetrahydro-2H-pyran-2-yl)oxy]-,
[4,4-bis[bis(1-methylethoxy)phosphinyl]butyl]carbamate,
(1α,3β,5Z,7E)- (9CI) (CA INDEX NAME)

PAGE 1-B

RN 211866-13-6 HCAPLUS

CN 9,10-Secocholesta-5,7,10(19)-triene-1,3-diol, 25-[(tetrahydro-2H-pyran-2-yl)oxy]-, 1-[[4,4-bis[bis(1-methylethoxy)phosphinyl]butyl]carbamate], $(1\alpha,3\beta,5Z,7E)$ - (9CI) (CA INDEX NAME)

PAGE 1-B

RN 211866-15-8 HCAPLUS

ON 9,10-Secocholesta-5,7,10(19)-trien-3-ol, 1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-25-[(tetrahydro-2H-pyran-2-yl)oxy]-, carbonochloridate, (1α,3β,5Z,7E)- (9CI) (CA INDEX NAME)

RN 211866-16-9 HCAPLUS
CN 9,10-Secocholesta-5,7,10(19)-trien-3-ol, 1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-25-[(tetrahydro-2H-pyran-2-yl)oxy]-,
 [4,4-bis[bis(1-methylethoxy)phosphinyl]butyl]carbamate,
 (1α,3β,5Z,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 211866-17-0 HCAPLUS 9,10-Secocholesta-5,7,10(19)-triene-1,3-diol, 25-[(tetrahydro-2H-pyran-2-yl)oxy]-, 3-[[4,4-bis[bis(1-methylethoxy)phosphinyl]butyl]carbamate], $(1\alpha,3\beta,5Z,7E)$ - (9CI) (CA INDEX NAME)

RN 211866-19-2 HCAPLUS

CN 9,10-Secocholesta-5,7,10(19)-trien-25-ol, 1,3-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-, carbonochloridate, $(1\alpha,3\beta,5Z,7E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

RN 211866-20-5 HCAPLUS

CN 9,10-Secocholesta-5,7,10(19)-trien-25-ol, 1,3-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-, [2,2-bis[bis(1-methylethoxy)phosphinyl]ethyl]carbamate, $(1\alpha,3\beta,5Z,7E)$ - (9CI) (CA INDEX NAME)

PAGE 1-B

CN

RN 211866-21-6 HCAPLUS

9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 25-[2,2-bis[bis(1-methylethoxy)phosphinyl]ethyl]carbamate, $(1\alpha,3\beta,5Z,7E)$ - (9CI) (CA INDEX NAME)

PAGE 1-B

__OPr-i

RN 211866-00-1 HCAPLUS

CN 9,10-Secoergosta-5,7,10(19),22-tetraene-1,3,24-triol, 1-[(4,4-diphosphonobutyl)carbamate], (1α,3β,5Z,7E,22E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

PAGE 1-B

RN 211866-05-6 HCAPLUS

CN 9,10-Secoergosta-5,7,10(19),22-tetraene-1,3,24-triol, 3-[(4,4-diphosphonobuty1)carbamate], $(1\alpha,3\beta,5Z,7E,22E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 211866-14-7 HCAPLUS

CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 1-[(4,4-diphosphonobutyl)carbamate], $(1\alpha,3\beta,5Z,7E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

PAGE 1-A

PAGE 1-B

RN 211866-18-1 HCAPLUS

CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 3-[(4,4-diphosphonobutyl)carbamate], $(1\alpha,3\beta,5Z,7E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 211866-22-7 HCAPLUS

CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 25-[(2,2-diphosphonoethyl)carbamate], $(1\alpha,3\beta,5Z,7E)$ - (9CI) (CA INDEX NAME)

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L32 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN
     1997:4586 HCAPLUS
AN
DN
     126:26826
ED
     Entered STN: 06 Jan 1997
TI
     Vitamin D derivative and bisphosphonates for treatment of hypercalcemia
IN
     Endo, Koichi
PΑ
     Chugai Pharmaceutical Co Ltd, Japan
so
     Jpn. Kokai Tokkyo Koho, 5 pp.
     CODEN: JKXXAF
DT
     Patent
LΑ
     Japanese
IC
     ICM A61K031-66
     ICS A61K031-59
CC
     1-6 (Pharmacology)
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FAN.CNT 1

T 1 774	CIVI									
	PATENT NO.	KIND	DATE		APPLICA	ATION NO.		DATE		
							·			
PI	JP 08277223		A2	199610	22	JP 1996	-22543		19960208	<
PRAI	JP 1995-204	78		199502	208 <					
CLAS	S									
PAT	ENT NO.	CLASS	PATENT	FAMILY	CLASS	FICATIO	N CODES			
								- 		
JP (08277223	ICM	A61K031	66						
		ICS	A61K031	-59						

GI

AB Therapeutic agents for hypercalcemia contain vitamin D derivative I and/or bisphosphonates as active ingredients. Nude mice with hypercalcemia associated with cancer induced by transplantation of human pancreatic cancer cells were administered with I at 5 μ g/kg i.v. on day 0 and with pamidronate at 10 mg/kg i.v. on day 1 showing blood Ca2+ level of .apprx.1.4 mmol/L on day 3, vs. .apprx.2.1 mmol/L, for controls administered with solvents instead.

ST vitamin D analog bisphosphonate hypercalcemia treatment; cancer hypercalcemia treatment vitamin D analog; pamidronate vitamin D analog hypercalcemia treatment

IT 7440-70-2, Calcium, biological studies

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (humoral hypercalcemia of malignancy; vitamin D derivative and bisphosphonates for treatment of hypercalcemia associated with cancer)

IT 7440-70-2, Calcium, biological studies

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (hypercalcemia; vitamin D derivative and bisphosphonates for treatment of hypercalcemia associated with cancer)

IT 40391-99-9 103909-75-7

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(vitamin D derivative and bisphosphonates for treatment of hypercalcemia associated with cancer)

IT 40391-99-9 103909-75-7

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(vitamin D derivative and bisphosphonates for treatment of hypercalcemia associated with cancer)

RN 40391-99-9 HCAPLUS

CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{OH} \\ | \\ \text{H}_2\text{O}_3\text{P} - \text{C} - \text{CH}_2 - \text{CH}_2 - \text{NH}_2 \\ | \\ \text{PO}_3\text{H}_2 \end{array}$$

RN 103909-75-7 HCAPLUS

CN 1,3-Cyclohexanediol, 4-methylene-5-[(2E)-[(1S,3aS,7aS)-octahydro-1-[(1S)-1-

DATE

(3-hydroxy-3-methylbutoxy)ethyl]-7a-methyl-4H-inden-4-ylidene]ethylidene]-, (1R,3S,5Z)- (9CI) (CA INDEX NAME)

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L32 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN
     1986:161993 HCAPLUS
AN
     104:161993
DN
ED
     Entered STN: 17 May 1986
     Kit for use in the treatment of osteoporosis
ΤI
     Uchtman, Vernon Albert
IN
     Procter and Gamble Co., USA
PA
so
     Eur. Pat. Appl., 22 pp.
     CODEN: EPXXDW
DT
     Patent
LA
     English
IC
     ICM A61K031-66
     ICS A61K033-42; A61K031-59
CC
     1-10 (Pharmacology)
     Section cross-reference(s): 2
FAN.CNT 1
     PATENT NO.
                       · KIND
                                DATE
                                            APPLICATION NO.
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	CA	1277233		A1	19901204	CA 1985-480203	19850426 <
	ΑU	8541769		A1	19851107	AU 1985-41769	19850429 <
	ΑU	584611		B2	19890601		
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	DK	173735		B1	20010820		
	JP	61033117		A2	19860217	JP 1985-93506	19850430 <
	JP	06055675		B4	19940727		
	IL	76043		A1	19900429	IL 1985-76043	19850808 <
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	EP	381296		A 1	19900808	EP 1990-200433	19900223 <
	ΕP	381296		B1	19941130		
		R: AT,	BE, CH	, DE, F	R, GB, IT,	LI, LU, NL, SE	
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	US	1984-684	560	Α	19841221	<	
	ΕP	1985-200	650	Α	19850425	<	
CLASS							
PATENT		NO.	CLASS	PATENT	FAMILY CL	ASSIFICATION CODES	

EP 162510 ICM A61K031-66

ICS A61K031-59

AB A regimen kit is described for the treatment of osteoporosis which consists of a bone cell-activating compound (e.g., PO43-, 1,25-dihydroxyvitamin D3, F-, thyroxine, triiodothyronine, PGE2), a bone resorption-inhibiting polyphosphonate, and a nutrient supplement (e.g., Ca, vitamin D), or placebo in sequential administration. For example, patients clin. diagnosed for osteoporosis were treated with 3-8 cycles of regimen in which each cycle consists of 2 tablets (500 mg P each) of phosphate 3 times/day for 3 days, of di-Na ethane-1-hydroxy-1,1-diphosphonate (5 mg/kg/day divided in 3 doses) for 14 days, and remaining 73 days a diet containing ≥1 g Ca/day. All the patients exhibited significant improvement in osteoporotic conditions.

ST osteoporosis treatment phosphate polyphosphonate

IT Osteoporosis

(treatment of, regimen kit for)

IT 51-48-9, biological studies 363-24-6 1406-16-2 2809-21-4 6893-02-3 7414-83-7 7440-70-2, biological studies 10596-23-3 12583-68-5 13598-36-2D, derivs. 14265-44-2, biological studies 16984-48-8, biological studies 19356-17-3 32222-06-3

40391-99-9 66376-36-1 79778-41-9

RL: BIOL (Biological study)

(osteoporosis treatment with, regimen kit for)

IT 19356-17-3 32222-06-3 40391-99-9

66376-36-1 79778-41-9

RL: BIOL (Biological study)

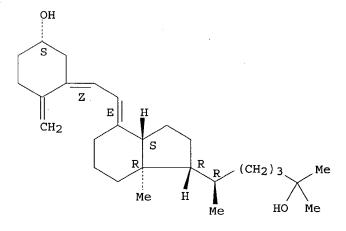
(osteoporosis treatment with, regimen kit for)

RN 19356-17-3 HCAPLUS

CN 9,10-Secocholesta-5,7,10(19)-triene-3,25-diol, (3β,5Z,7E)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



RN 32222-06-3 HCAPLUS

CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, $(1\alpha,3\beta,5Z,7E)$ -(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+). Double bond geometry as shown.

RN 40391-99-9 HCAPLUS

CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{OH} \\ | \\ \text{H}_2\text{O}_3\text{P} - \text{C} - \text{CH}_2 - \text{CH}_2 - \text{NH}_2 \\ | \\ \text{PO}_3\text{H}_2 \end{array}$$

RN 66376-36-1 HCAPLUS

CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)

$$^{\text{OH}}_{\text{H}_2\text{O}_3\text{P}-\text{C}-\text{(CH}_2)}^{\text{OH}}_{_3-\text{NH}_2}^{\text{PO}_3\text{H}_2}$$

RN 79778-41-9 HCAPLUS

CN Phosphonic acid, (6-amino-1-hydroxyhexylidene)bis- (9CI) (CA INDEX NAME)

$$^{OH}_{|}$$
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L32 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1986:103088 HCAPLUS

DN 104:103088

ED Entered STN: 05 Apr 1986

TI Contrasting effects of 1,25(OH)2 vitamin D3 and aminohydroxypropylidene diphosphonate (APD) on bone turnover in the mouse

AU Marie, P. J.; Hott, M.; Garba, M. T.

CS Hop. Lariboisiere, Paris, 75010, Fr.

SO Proceedings of the Workshop on Vitamin D (1985), 6th(Vitam. D), 481-2

CODEN: PWVDDU; ISSN: 0721-7110

```
DT
     Journal
     English
LA
CC
     2-9 (Mammalian Hormones)
                                    [32222-06-3] administration to
     1,25-Dihydroxyvitamin D3 (I)
AB
     37-day-old mice decreased body and skeletal growth, and these effects were
     antagonized by aminohydroxypropylidene diphosphonate (APD)
     40391-99-9]. ADP also prevented the hypercalcemic effects of I.
     Addnl., bone mineralization was not augmented after treatment with ADP and
     I despite increasing circulating I levels. Thus, the stimulatory effect of I on bone mineralization is blocked when bone resorption is inhibited,
     suggesting that I promotes bone mineralization mainly in response to
     stimulation of bone resorption.
     dihydroxyvitamin D3 bone resorption mineralization;
ST
     aminohydroxypropylidene diphosphonate bone metab
IT
     Blood serum
         (calcium of, dihydroxyvitamin D3 effect on, aminohydroxypropylidene
        diphosphonate in relation to)
IT
     Osteoclast
         (dihydroxyvitamin D3 effect on, aminohydroxypropylidene diphosphonate
        modulation of, bone resorption in relation to)
IT
     Bone, metabolism
         (mineralization and resorption of, dihydroxyvitamin D3 effect on)
IT
     Resorption
         (of bone, dihydroxyvitamin D3 effect on, mineralization in relation to)
IT
     40391-99-9
     RL: BIOL (Biological study)
         (bone metabolism response to dihydroxyvitamin D3 and)
IT
     32222-06-3
     RL: BIOL (Biological study)
         (bone metabolism response to, aminohydroxypropylidene diphosphonate effect
        on)
TT
     7440-70-2, biological studies
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
         (metabolism of, by bone, dihydroxyvitamin D3 effect on,
        aminohydroxypropylidene diphosphonate in relation to)
IT
     40391-99-9
     RL: BIOL (Biological study)
         (bone metabolism response to dihydroxyvitamin D3 and)
RN
     40391-99-9 HCAPLUS
     Phosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX NAME)
CN
       OH
H2O3P-C-CH2-CH2-NH2
       PO<sub>3</sub>H<sub>2</sub>
IT
     32222-06-3
     RL: BIOL (Biological study)
         (bone metabolism response to, aminohydroxypropylidene diphosphonate effect
RN
     32222-06-3 HCAPLUS
CN
     9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, (1\alpha,3\beta,5Z,7E)-
              (CA INDEX NAME)
Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.
```

HO
$$\frac{Z}{Z}$$
 E $\frac{H}{S}$ $\frac{R}{Me}$ $\frac{R}{Me}$ $\frac{CH_2}{HO}$ $\frac{3}{Me}$ $\frac{Me}{Me}$

```
L32 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN
    1986:45761 HCAPLUS
AN
DN
    104:45761
ED
    Entered STN: 23 Feb 1986
ΤI
    Use of a two- or multiphase agent for treating or preventing osteoporosis
IN
    Flora, Lawrence
```

PΑ Procter and Gamble Co., USA

Ger. Offen., 22 pp. SO

CODEN: GWXXBX

DTPatent

LA German

ICM A61K031-66 IC

ICS A61K031-59; A61K037-24; A61K031-557

1-12 (Pharmacology) CC

FAN.CNT 1

F	AN, CNI I				
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
		-			
P	I DE 3514584	A1	19851031	DE 1985-3514584	19850423 <
	AU 8541484	A1	19851107	AU 1985-41484	19850422 <
	AU 569391	B2	19880128		
	BE 902308	A1	19851029	BE 1985-214929	19850429 <
	US 4822609	Α	19890418	US 1986-906725	19860912 <
P	RAI US 1984-605541		19840430	<	
	US 1984-684542		19841221	<	
C	LASS				

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
DE 3514584	ICM	A61K031-66

A61K031-59; A61K037-24; A61K031-557 AB

Osteoporosis is treated by the administration of a bone-cell-activating agent, such as inorg. phosphate, 1,25-dihydroxyvitamin D3, 25-hydroxyvitamin D3, etc., in the 1st stage, followed by the administration of a bone resorption-inhibiting polyphosphonate in the 2nd stage, and the administration of Ca and vitamin D in the 3rd stage. Thus, osteoporotic patients were given phosphate tablets (500 mg P), 3 times per day, for 3 days, followed by the administration of Didronel (5 mg/kg/day) for 14 days. Subsequently, >1 g Ca/day was administered for 45 days. The cycles were repeated 3-8 times. A decrease in the intensity of osteoporosis was observed

STosteoporosis treatment phosphate polyphosphonate; bone resorption inhibition osteoporosis treatment

ITPhosphates, biological studies

RL: BIOL (Biological study)

(osteoporosis treatment by bone resorption-inhibiting polyphosphonates

and) ΙT Osteoporosis (treatment of, by bone cell-activating and bone resorption-inhibiting 1406-16-2 ΙT 7440-70-2, biological studies RL: BIOL (Biological study) (in treatment of osteoporosis) IT 2809-21-4 10596-23-3 40391-99-9 66376-36-1 79778-41-9 RL: BIOL (Biological study) (osteoporosis treatment by bone cell-activating agents and) IT51-48-9, biological studies 363-24-6 6893-02-3 16984-48-8, biological studies 19356-17-3 32222-06-3 RL: BIOL (Biological study) (osteoporosis treatment by bone resorption-inhibiting polyphosphonates IT40391-99-9 66376-36-1 79778-41-9 RL: BIOL (Biological study) (osteoporosis treatment by bone cell-activating agents and) RN40391-99-9 HCAPLUS CNPhosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX NAME) OH $H_2O_3P-C-CH_2-CH_2-NH_2$ PO3H2 RN66376-36-1 HCAPLUS Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME) CNOH $H_2O_3P-C-(CH_2)_3-NH_2$ PO3H2 RN79778-41-9 HCAPLUS Phosphonic acid, (6-amino-1-hydroxyhexylidene)bis- (9CI) (CA INDEX NAME) CNOH $H_2O_3P-C-(CH_2)_5-NH_2$ PO_3H_2 IT19356-17-3 32222-06-3 RL: BIOL (Biological study) (osteoporosis treatment by bone resorption-inhibiting polyphosphonates

9,10-Secocholesta-5,7,10(19)-triene-3,25-diol, (3β,5Z,7E)- (9CI)

Absolute stereochemistry.

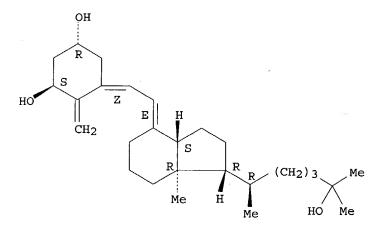
Double bond geometry as shown.

INDEX NAME)

19356-17-3 HCAPLUS

RN CN

Absolute stereochemistry. Rotation (+). Double bond geometry as shown.



L32 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1986:45760 HCAPLUS

DN 104:45760

ED Entered STN: 23 Feb 1986

TI Multistage method for treating or preventing osteoporosis

IN Anderson, Colin; Flora, Lawrence

PA Procter and Gamble Co., USA

SO Ger. Offen., 23 pp.

CODEN: GWXXBX

DT Patent

LA German

IC ICM A61K031-66

ICS A61K031-59; A61K037-24; A61K031-557

CC 1-12 (Pharmacology)

FAN CNT 1

FAN.CNT I					
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ΡI	DE 3514583	A1	19851031	DE 1985-3514583	19850423 <
	AU 8541619	A1	19851107	AU 1985-41619	19850423 <
	AU 568433	B2	19871224		
	BE 902307	A1	19851029	BE 1985-214928	19850429 <

US 1986-906858 US 4812304 19890314 19860912 <--PRAI US 1984-605539 19840430 <--US 1984-684541 19841221 CLASS PATENT NO. CLASS PATENT FAMILY CLASSIFICATION CODES ----DE 3514583 ICM A61K031-66 ICS A61K031-59; A61K037-24; A61K031-557 AΒ The 1st stage of the title treatment consists of daily administration of a bone-cell-activating drug, such as 1,25-dihydroxyvitamin D3, inorg. fluoride, inorg. phosphate, etc. The 2nd stage, a bone absorption-inhibitor, such as ethane-1-hydroxy-1,1-diphosphonic acid, is administered. Ca and vitamin D are given in the 3rd stage. Thus, osteoporotic patients were given 2 tablets of inorg. phosphate (500 mg P/tablet), 3 times/day, for 3 days. Subsequently, Didronel (EHDP-Na2) (5 mg/kg/day) was administered for 14 days, followed by 73 days on a diet containing >1 g Ca/day. Remission of osteoporosis was shown by microscopic examination of bioptic samples after several treatment cycles. ST osteoporosis treatment; bone absorption inhibitor osteoporosis treatment IT Osteoporosis (treatment of, with bone cell-stimulating and bone absorptioninhibiting agents) IT 2809-21-4 10596-23-3 40391-99-9 66376-36-1 79778-41-9 RL: BIOL (Biological study) (bone absorption-inhibiting agent, in osteoporosis treatment) 51-48-9, biological studies 363-24-6 6893-02-3 7414-83-7 IT 7681-49-4, biological studies 9002-64-6 16984-48-8, biological studies 19356-17-3 32222-06-3 RL: BIOL (Biological study) (bone cell-activating agent, in osteoporosis treatment) 1406-16-2 7440-70-2, biological studies TT RL: BIOL (Biological study) (in osteoporosis treatment) IT 40391-99-9 66376-36-1 79778-41-9 RL: BIOL (Biological study) (bone absorption-inhibiting agent, in osteoporosis treatment) RN 40391-99-9 HCAPLUS CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX NAME) ОН $H_2O_3P-C-CH_2-CH_2-NH_2$ PO₃H₂ 66376-36-1 HCAPLUS RN CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME) OH $H_2O_3P-C-(CH_2)_3-NH_2$ PO3H2

RN 79778-41-9 HCAPLUS CN Phosphonic acid, (6-amino-1-hydroxyhexylidene)bis- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{OH} \\ | \\ \text{H}_2\text{O}_3\text{P-C-(CH}_2)}_5 - \text{NH}_2 \\ | \\ \text{PO}_3\text{H}_2 \end{array}$$

IT 19356-17-3 32222-06-3

RL: BIOL (Biological study)

(bone cell-activating agent, in osteoporosis treatment)

RN 19356-17-3 HCAPLUS

CN 9,10-Secocholesta-5,7,10(19)-triene-3,25-diol, (3β,5Z,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 32222-06-3 HCAPLUS

CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, $(1\alpha,3\beta,5Z,7E)$ -(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+). Double bond geometry as shown.

L32 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1985:554780 HCAPLUS

DN 103:154780

ED Entered STN: 16 Nov 1985

TIInhibition by aminohydroxypropylidene bisphosphonate (AHPrBP) of 1,25-dihydroxyvitamin D3-induced stimulated bone turnover in the mouse AU Marie, Pierre J.; Hott, Monique; Garba, Marie Therese INSERM, Hop. Lariboisiere, Paris, 75010, Fr. CS Calcified Tissue International (1985), 37(3), 268-75 SO CODEN: CTINDZ; ISSN: 0171-967X DTJournal English LA CC2-9 (Mammalian Hormones) 1,25-Dihydroxyvitamin D3 [1,25(OH)2D3] [32222-06-3]-induced AΒ increased bone mineralization in the mouse was evaluated in relation to stimulation of bone resorption. To inhibit bone resorption, 35-day-old mice were given 16 µmol/kg/day of (3-amino-1-hydroxypropylidene)-1,1biphosphonate (AHPrBP) [40391-99-9] for 10 days, the 1st injection occurring 3 days prior to the continuous infusion of 0.006, 0.13, or 0.20 μ g/kg/day of 1,25(OH)2D3 for 7 days. Two groups of mice were treated with AHPrBP or 1,25(OH) 2D3 alone. The skeletal changes were assessed by histomorphometric study of caudal vertebrae after double [3H]proline and double tetracycline labelings for evaluation of the matrix apposition rate(MaAR) and mineral apposition rate(MiAR), resp. Treatment with AHPrBP alone or combined with 1,25 (OH) 2D3 decreased the number of acid phosphatase [9001-77-8]-stained osteoclasts and reduced the endosteal MaAR and MiAR and the amount of osteoid. When given alone, 1,25(OH)2D3 increased serum Ca above normal, enhanced the number of histochem. active osteoclasts, and stimulated the endosteal MiAR. Pretreatment with AHPrBP blocked both the increase in serum Ca and the stimulation of the MirAR induced by 1,25(OH)2D3 infusion though serum 1,25(OH)2D3 levels rose according to the dose given. The serum Ca and the bone resorbing responses to 1,25(OH)2D3 infusion are prevented by pretreatment with AHPrBP, and the stimulatory effects of 1,25(OH)2D3 on the mineralization rate is blocked when bone resorption is inhibited. Evidently, 1,25(OH)2D3 promotes bone mineralization in the mouse mainly in response to stimulation of bone resorption. STvitamin D bone mineralization resorption; dihydroxycholecalciferol bone mineralization resorption Osteoclast IΤ (acid phosphatase of, in dihydroxyvitamin D3-induced bone mineralization, bone resorption in relation to) IT (calcium of, in dihydroxyvitamin D3-induced bone mineralization, bone resorption in relation to) IT Bone, metabolism (mineralization of, dihydroxyvitamin D3 effect on, resorption in relation to) IT Resorption (of bone, dihydroxyvitamin D3-induced mineralization in relation to) IT 32222-06-3 RL: BIOL (Biological study) (bone mineralization stimulation by, bone resorption in relation to) IT 40391-99-9 RL: BIOL (Biological study) (bone resorption inhibition by, dihydroxyvitamin D3 effect on bone mineralization in) 7440-70-2, biological studies IT RL: BIOL (Biological study) (of blood serum, in dihydroxyvitamin D3-induced bone mineralization, bone resorption in relation to) TT 9001-77-8 RL: BIOL (Biological study) (of osteoclasts, in dihydroxyvitamin D3-induced bone mineralization, bone resorption in relation to) IT 32222-06-3

RL: BIOL (Biological study)

(bone mineralization stimulation by, bone resorption in relation to) RN 32222-06-3 HCAPLUS CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, $(1\alpha,3\beta,5Z,7E)$ -(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+). Double bond geometry as shown.

IT 40391-99-9

RL: BIOL (Biological study)

(bone resorption inhibition by, dihydroxyvitamin D3 effect on bone mineralization in)

RN 40391-99-9 HCAPLUS

CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX NAME)

=> fil uspatall

FILE 'USPATFULL' ENTERED AT 10:42:01 ON 16 NOV 2004 CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPAT2' ENTERED AT 10:42:01 ON 16 NOV 2004 CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

=> => d 140 bib abs kwic hitstr tot

L40 ANSWER 1 OF 6 USPATFULL on STN

AN 2003:187408 USPATFULL

TI Targeted therapeutic delivery of vitamin D compounds

IN Mazess, Richard B., Madison, WI, UNITED STATES Bishop, Charles W., Madison, WI, UNITED STATES

PA Bone Care International, Inc., Middleton, WI (U.S. corporation)

PI US 2003129194 A1 20030710

AI US 2002-251905 A1 20020920 (10)

RLI Continuation-in-part of Ser. No. US 2000-402636, filed on 26 Apr 2000, PENDING A 371 of International Ser. No. WO 1998-US2899, filed on 13 Feb 1998, PENDING

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PRAI US 1997-38364P 19970213 (60)

```
DT
       Utility
FS
       APPLICATION
LREP
       MICHAEL BEST & FRIEDRICH, LLP, ONE SOUTH PINCKNEY STREET, P O BOX 1806,
       MADISON, WI, 53701
       Number of Claims: 57
CLMN
ECL
       Exemplary Claim: 1
DRWN
       9 Drawing Page(s)
LN.CNT 1655
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       The present invention is directed to a conjugate which includes at least
       one vitamin D moiety thereof and at least one targeting molecule moiety
       to pharmaceutical compositions of the conjugate, and to methods for
       using the conjugate for target-specific delivery of vitamin D or analogs
       thereof to tissues in need thereof. When a particularly preferred form
       is administered to a patient, the targeting molecule component of the
       conjugate of this invention seeks out and binds to a tissue of interest,
       such as bone or tumor tissue, where the vitamin D has a therapeutic
       effect.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PRAI
       US 1997-38364P
                           19970213 (60)
          . . Examples of bisphosphonates include, but are not limited to
DETD
       1-hydroxyethylidene-1,1-bisphosphonic ligand (etidronate),
       dichloromethylene bisphosphonic acid ligand, 3-amino-1-
       hydroxypropylidene-1-bisphosphonic acid ligand (pamidronate),
       alendronate, clodronate, ibandronate, rosedronate,
       tiludronate, zoledronate, and combinations thereof. For
       example, a specific bisphosphonate moiety which is suitably operable in
       the present invention is represented by.
CLM
       What is claimed is:
       33. A method as set forth in claim 34, wherein the bisphosphonate
       includes at least one of alendronate, clodronate, etidronate,
       ibandronate, pamidronate, risedronate, tiludronate,
       zoledronate and combinations thereof.
IT
      107-30-2, Chloromethyl methyl ether
                                            70550-73-1 211865-86-0
        (targeted therapeutic delivery of vitamin D compds.)
IT
      81522-68-1P 140710-96-9P 144034-23-1P
      211865-87-1P 211865-88-2P 211865-89-3P
      211865-90-6P 211865-92-8P 211865-93-9P
      211865-94-0P 211865-96-2P 211865-97-3P
      211865-98-4P 211865-99-5P 211866-01-2P
      211866-02-3P 211866-03-4P 211866-04-5P
      211866-06-7P 211866-07-8P 211866-08-9P
      211866-09-0P 211866-11-4P 211866-12-5P
      211866-13-6P 211866-15-8P 211866-16-9P
      211866-17-0P 211866-19-2P 557072-52-3P
      557072-53-4P
        (targeted therapeutic delivery of vitamin D compds.)
IT
    211865-95-1P
        (targeted therapeutic delivery of vitamin D compds.)
IT
    211866-10-3P
        (targeted therapeutic delivery of vitamin D compds.)
IT
    211865-91-7P 211866-00-1P 211866-05-6P
      211866-14-7P 211866-18-1P 557072-54-5P
        (targeted therapeutic delivery of vitamin D compds.)
IT
      1406-16-2D, Vitamin d, conjugates
                                          2809-21-4 10596-23-3
      32222-06-3, 1\alpha, 25-Dihydroxyvitamin D3 40391-99-9
      41294-56-8, 1\alpha-Hydroxyvitamin D3 54573-75-0,
      1\alpha-Hydroxyvitamin D2 60133-18-8, 1\alpha, 25-
      Dihydroxyvitamin D2 66376-36-1, Alendronate 83805-11-2
                        89987-06-4, Tiludronate 103909-75-7,
      , Falecalcitriol
```

Maxacalcitol 105462-24-6 112965-21-6, Calcipotriol

Absolute stereochemistry.
Double bond geometry as shown.

140710-96-9P 144034-23-1P 211865-87-1P 211865-88-2P 211865-89-3P 211865-90-6P 211865-92-8P 211865-93-9P 211865-94-0P 211865-96-2P 211865-97-3P 211865-98-4P 211865-99-5P 211866-01-2P 211866-02-3P 211866-03-4P 211866-04-5P 211866-07-8P 211866-08-9P 211866-09-0P 211866-11-4P 211866-12-5P 211866-13-6P 211866-15-8P 211866-16-9P 211866-17-0P 211866-19-2P 557072-52-3P 557072-53-4P (targeted therapeutic delivery of vitamin D compds.) 140710-96-9 USPATFULL RNCN9,10-Secocholesta-5,7,10(19)-trien-25-ol, 1,3-bis[[(1,1dimethylethyl) dimethylsilyl] α , $(1\alpha, 3\beta, 5Z, 7E)$ - (9CI) (CA INDEX NAME)

RN144034-23-1 USPATFULL

CNPhosphonic acid, (4-aminobutylidene)bis-, tetrakis(1-methylethyl) ester (9CI) (CA INDEX NAME)

RN 211865-87-1 USPATFULL

CN9,10-Secoergosta-5,7,10(19),22-tetraen-24-ol, 1,3-bis[[(1,1dimethylethyl)dimethylsilyl]oxy]-, carbonochloridate, $(1\alpha, 3\beta, 5E, 7E, 22E)$ - (9CI) (CA INDEX NAME)

> Absolute stereochemistry. Double bond geometry as shown.

RN 211865-88-2 USPATFULL

CN

9,10-Secoergosta-5,7,10(19),22-tetraen-24-ol, 1,3-bis[[(1,1dimethylethyl)dimethylsilyl]oxy]-, [4,4-bis[bis(1methylethoxy) phosphinyl] butyl] carbamate, $(1\alpha, 3\beta, 5E, 7E, 22E)$ -(9CI) (CA INDEX NAME)

PAGE 1-B

RN 211865-89-3 USPATFULL

CN 9,10-Secoergosta-5,7,10(19),22-tetraene-1,3,24-triol, 24-[[4,4-bis[bis(1-methylethoxy)phosphinyl]butyl]carbamate], $(1\alpha,3\beta,5E,7E,22E)$ -(9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

PAGE 1-A

PAGE 1-B

RN

CN

211865-90-6 USPATFULL

9,10-Secoergosta-5,7,10(19),22-tetraene-1,3,24-triol, 24-[(4,4-diphosphonobutyl)carbamate] (9CI) (CA INDEX NAME)

RN 211865-92-8 USPATFULL

CN Silane, [[(1α , 3β , 5E, 7E, 22E) -24-(methoxymethoxy)-9,10-secoergosta-5,7,10(19),22-tetraene-1,3-diyl]bis(oxy)]bis[(1,1-dimethylethyl)dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 211865-93-9 USPATFULL

CN 9,10-Secoergosta-5,7,10(19),22-tetraene-1,3-diol, 24-(methoxymethoxy)-, $(1\alpha,3\beta,5E,7E,22E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 211865-94-0 USPATFULL

CN 9,10-Secoergosta-5,7,10(19),22-tetraen-1-ol, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-24-(methoxymethoxy)-, $(1\alpha,3\beta,5E,7E,22E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 211865-96-2 USPATFULL

Absolute stereochemistry.

Double bond geometry as shown.

RN 211865-97-3 USPATFULL

CN 9,10-Secoergosta-5,7,10(19),22-tetraen-1-ol, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-24-(methoxymethoxy)-,
 [4,4-bis[bis(1-methylethoxy)phosphinyl]butyl]carbamate,
 (1α,3β,5E,7E,22E)- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

RN 211865-98-4 USPATFULL CN 9,10-Secoergosta-5,7,10

9,10-Secoergosta-5,7,10(19),22-tetraene-1,3-diol, 24-(methoxymethoxy)-, 1-[[4,4-bis[bis(1-methylethoxy)phosphinyl]butyl]carbamate], $(1\alpha,3\beta,5E,7E,22E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

PAGE 1-A

PAGE 1-B

RN 211865-99-5 USPATFULL

CN 9,10-Secoergosta-5,7,10(19),22-tetraene-1,3,24-triol, 1-[(4,4-diphosphonobutyl)carbamate], $(1\alpha,3\beta,5E,7E,22E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

PAGE 1-A

PAGE 1-B

__pr-i

RN 211866-01-2 USPATFULL

RN 211866-02-3 USPATFULL

CN 9,10-Secoergosta-5,7,10(19),22-tetraen-3-ol, 1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-24-(methoxymethoxy)-, [4,4-bis[bis(1-methylethoxy)phosphinyl]butyl]carbamate, $(1\alpha,3\beta,5E,7E,22E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

PAGE 1-B

Ме

PAGE 1-A

OMe

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OPr-i

RN 211866-03-4 USPATFULL

CN 9,10-Secoergosta-5,7,10(19),22-tetraene-1,3-diol, 24-(methoxymethoxy)-, $3-[[4,4-bis[bis(1-methylethoxy)phosphinyl]butyl]carbamate], (1\alpha,3\beta,5E,7E,22E)- (9CI) (CA INDEX NAME)$

PAGE 1-A

PAGE 1-B

OMe

RN 211866-04-5 USPATFULL

CN 9,10-Secoergosta-5,7,10(19),22-tetraene-1,3,24-triol, 3-[(4,4-diphosphonobutyl)carbamate], $(1\alpha,3\beta,5E,7E,22E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 211866-07-8 USPATFULL

CN Silane, [[(1α ,3 β ,5Z,7E)-25-[(tetrahydro-2H-pyran-2-yl)oxy]-9,10-secocholesta-5,7,10(19)-triene-1,3-diyl]bis(oxy)]bis[(1,1-dimethylethyl)dimethyl- (9CI) (CA INDEX NAME)

RN 211866-08-9 USPATFULL

CN 9,10-Secocholesta-5,7,10(19)-triene-1,3-diol, 25-[(tetrahydro-2H-pyran-2-yl)oxy]-, $(1\alpha,3\beta,5z,7E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 211866-09-0 USPATFULL

CN 9,10-Secocholesta-5,7,10(19)-trien-1-ol, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-25-[(tetrahydro-2H-pyran-2-yl)oxy]-, $(1\alpha,3\beta,5Z,7E)$ - (9CI) (CA INDEX NAME)

RN 211866-11-4 USPATFULL

CN 9,10-Secocholesta-5,7,10(19)-trien-1-ol, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-25-[(tetrahydro-2H-pyran-2-yl)oxy]-, carbonochloridate, $(1\alpha,3\beta,5Z,7E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

RN 211866-12-5 USPATFULL

PAGE 1-A

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RN 211866-13-6 USPATFULL

CN 9,10-Secocholesta-5,7,10(19)-triene-1,3-diol, 25-[(tetrahydro-2H-pyran-2-yl)oxy]-, 1-[[4,4-bis[bis(1-methylethoxy)phosphinyl]butyl]carbamate], $(1\alpha,3\beta,5Z,7E)$ - (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

CN

RN 211866-15-8 USPATFULL

9,10-Secocholesta-5,7,10(19)-trien-3-ol, 1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-25-[(tetrahydro-2H-pyran-2-yl)oxy]-, carbonochloridate, $(1\alpha,3\beta,5Z,7E)$ - (9CI) (CA INDEX NAME)

RN 211866-16-9 USPATFULL

Absolute stereochemistry.

Double bond geometry as shown.

RN 211866-17-0 USPATFULL

CN 9,10-Secocholesta-5,7,10(19)-triene-1,3-diol, 25-[(tetrahydro-2H-pyran-2-yl)oxy]-, 3-[[4,4-bis[bis(1-methylethoxy)phosphinyl]butyl]carbamate], $(1\alpha,3\beta,5Z,7E)$ - (9CI) (CA INDEX NAME)

RN 211866-19-2 USPATFULL

CN 9,10-Secocholesta-5,7,10(19)-trien-25-ol, 1,3-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-, carbonochloridate, $(1\alpha,3\beta,5Z,7E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 557072-52-3 USPATFULL

CN 9,10-Secocholesta-5,7,10(19)-trien-25-ol, 1,3-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-, [4,4-bis[bis(1-methylethoxy)phosphinyl]butyl]carbamate, $(1\alpha,3\beta,5Z,7E)$ - (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

RN 557072-53-4 USPATFULL

PAGE 1-A

PAGE 1-B

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OPr-i
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OPr-i

IT 211865-95-1P

(targeted therapeutic delivery of vitamin D compds.)
RN 211865-95-1 USPATFULL
CN 9,10-Secoergosta-5,7,10(19),22-tetraen-3-ol, 1-[[(1,1-

9,10-Secoergosta-5,7,10(19),22-tetraen-3-ol, 1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-24-(methoxymethoxy)-, $(1\alpha,3\beta,5E,7E,22E)$ - (9CI) (CA INDEX NAME)

IT 211866-10-3P

(targeted therapeutic delivery of vitamin D compds.)

RN 211866-10-3 USPATFULL

Absolute stereochemistry.

Double bond geometry as shown.

IT 211865-91-7P 211866-00-1P 211866-05-6P

211866-14-7P 211866-18-1P 557072-54-5P

(targeted therapeutic delivery of vitamin D compds.)

RN 211865-91-7 USPATFULL

CN 9,10-Secoergosta-5,7,10(19),22-tetraene-1,3,24-triol, 24-[(4,4-diphosphonobutyl)carbamate], (1α,3β,5Z,7E,22E)- (9CI) (CA INDEX NAME)

RN 211866-00-1 USPATFULL

CN 9,10-Secoergosta-5,7,10(19),22-tetraene-1,3,24-triol, 1-[(4,4-diphosphonobutyl)carbamate], (1α,3β,5Z,7E,22E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

PAGE 1-A

$$H_{2O_3P}$$
 $(CH_2)_3$ N CH_2 E H R R E S Me Me Me Me Me

PAGE 1-B

RN 211866-05-6 USPATFULL

CN 9,10-Secoergosta-5,7,10(19),22-tetraene-1,3,24-triol, 3-[(4,4-diphosphonobutyl)carbamate], $(1\alpha,3\beta,5Z,7E,22E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

HO
$$\frac{(CH_2)_3}{PO_3H_2}$$
 $\frac{PO_3H_2}{R}$
 $\frac{E}{Me}$
 $\frac{H}{Me}$
 $\frac{R}{Me}$
 $\frac{R}{Me}$
 $\frac{R}{Me}$
 $\frac{R}{Me}$
 $\frac{R}{Me}$
 $\frac{R}{Me}$
 $\frac{R}{Me}$
 $\frac{R}{Me}$
 $\frac{R}{Me}$

RN 211866-14-7 USPATFULL

CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 1-[(4,4-diphosphonobutyl)carbamate], $(1\alpha,3\beta,5Z,7E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

PAGE 1-A

PAGE 1-B

RN 211866-18-1 USPATFULL

CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 3-[(4,4-diphosphonobutyl)carbamate], $(1\alpha,3\beta,5Z,7E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 557072-54-5 USPATFULL

CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 25-[(4,4-diphosphonobutyl)carbamate], $(1\alpha,3\beta,5Z,7E)$ - (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

— PO3H₂

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IT 32222-06-3, 1\alpha, 25-Dihydroxyvitamin D3 40391-99-9
      41294-56-8, 1\alpha-Hydroxyvitamin D3 54573-75-0, 1\alpha-Hydroxyvitamin D2 60133-18-8, 1\alpha, 25-
      Dihydroxyvitamin D2 66376-36-1, Alendronate 83805-11-2
       , Falecalcitriol 103909-75-7, Maxacalcitol 105462-24-6
      112965-21-6, Calcipotriol 114084-78-5, Ibandronate
      118072-93-8, Zoledronate 124043-51-2,
      1\alpha, 24-Dihydroxyvitamin D2 131249-38-2,
      1\alpha, 25-Dihydroxyvitamin D4 131918-61-1, Paricalcitol
      134404-52-7, Seocalcitol 157893-62-4,
      1\alpha, 24-Dihydroxyvitamin D4
         (targeted therapeutic delivery of vitamin D compds.)
     32222-06-3 USPATFULL
RN
CN
     9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, (1\alpha,3\beta,5Z,7E)-
         (9CI) (CA INDEX NAME)
       Absolute stereochemistry. Rotation (+).
       Double bond geometry as shown.
```

RN 40391-99-9 USPATFULL CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{OH} \\ | \\ \text{H}_2\text{O}_3\text{P--}\text{C---}\text{CH}_2\text{---}\text{CH}_2\text{---}\text{NH}_2 \\ | \\ \text{PO}_3\text{H}_2 \end{array}$$

RN 41294-56-8 USPATFULL CN 9,10-Secocholesta-5,7,10(19)-triene-1,3-diol, $(1\alpha,3\beta,5Z,7E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+). Double bond geometry as shown.

 $\begin{array}{lll} RN & 54573-75-0 & USPATFULL \\ CN & 9,10\text{-Secoergosta-5,7,10(19),22-tetraene-1,3-diol,} \\ & & (1\alpha,3\beta,5Z,7E,22E)- & (9CI) & (CA INDEX NAME) \\ \end{array}$

RN 60133-18-8 USPATFULL CN 9,10-Secoergosta-5,7,10(19),22-tetraene-1,3,25-triol, $(1\alpha,3\beta,5Z,7E,22E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 66376-36-1 USPATFULL CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)

RN 83805-11-2 USPATFULL

CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 26,26,26,27,27,27-hexafluoro-, (1α,3β,5Ζ,7Ε)- (9CI) (CA INDEX NAME)

RN 103909-75-7 USPATFULL

CN 1,3-Cyclohexanediol, 4-methylene-5-[(2E)-[(1S,3aS,7aS)-octahydro-1-[(1S)-1-(3-hydroxy-3-methylbutoxy)ethyl]-7a-methyl-4H-inden-4-ylidene]-, (1R,3S,5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 105462-24-6 USPATFULL

CN Phosphonic acid, [1-hydroxy-2-(3-pyridinyl)ethylidene]bis- (9CI) (CA INDEX NAME)

RN 112965-21-6 USPATFULL

CN 9,10-Secochola-5,7,10(19),22-tetraene-1,3,24-triol, 24-cyclopropyl-, (1α,3β,5Z,7E,22E,24S)- (9CI) (CA INDEX NAME)

RN 114084-78-5 USPATFULL
CN Phosphonic acid, [1-hydroxy-3-(methylpentylamino)propylidene]bis- (9CI)
(CA INDEX NAME)

$$\begin{array}{c|c} \text{OH} & \text{Me} \\ | & | \\ \text{H}_2\text{O}_3\text{P--}\text{C--}\text{CH}_2\text{--}\text{CH}_2\text{--}\text{N--} (\text{CH}_2)_4\text{---}\text{Me} \\ | & \\ \text{PO}_3\text{H}_2 \end{array}$$

RN 118072-93-8 USPATFULL CN Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis- (9CI) (CA INDEX NAME)

RN 124043-51-2 USPATFULL CN 9,10-Secoergosta-5,7,10(19),22-tetraene-1,3,24-triol, $(1\alpha,3\beta,5Z,7E,22E,24\xi)$ - (9CI) (CA INDEX NAME)

RN 131249-38-2 USPATFULL

CN 9,10-Secoergosta-5,7,10(19)-triene-1,3,25-triol, $(1\alpha,3\beta,5Z,7E)$ -(9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 131918-61-1 USPATFULL

CN 19-Nor-9,10-secoergosta-5,7,22-triene-1,3,25-triol, $(1\alpha,3\beta,7E,22E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 134404-52-7 USPATFULL

CN 1,3-Cyclohexanediol, 5-[(2E)-[(1R,3aS,7aR)-1-[(1R,2E,4E)-6-ethyl-6-hydroxy-1-methyl-2,4-octadienyl]octahydro-7a-methyl-4H-inden-4-ylidene]-4-methylene-, (1R,3S,5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

157893-62-4 USPATFULL RN

9,10-Secoergosta-5,7,10(19)-triene-1,3,24-triol, $(1\alpha,3\beta,5Z,7E)$ -CN (CA INDEX NAME)

> Absolute stereochemistry. Double bond geometry as shown.

ANSWER 2 OF 6 USPATFULL on STN L40 2002:325851 USPATFULL ANΤТ

Response element compositions and assays employing same

Sucov, Henry M., San Diego, CA, United States IN Evans, Ronald M., La Jolla, CA, United States Umesono, Kazuhiko, La Jolla, CA, United States

The Salk Institute for Biological Studies, La Jolla, CA, United States PA

(U.S. corporation) US 6492137 PΙ

20021210 В1

19910319 (7) US 1991-672530 AΙ

Continuation-in-part of Ser. No. US 1989-438757, filed on 16 Nov 1989, RLI now patented, Pat. No. US 5091518

 \mathbf{DT} Utility

FS GRANTED Primary Examiner: McKelvey, Terry EXNAM

LREP Reiter, Stephen E., Foley & Lardner CLMN Number of Claims: 32

ECL Exemplary Claim: 1

12 Drawing Figure(s); 5 Drawing Page(s) DRWN

LN.CNT 1395

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DNA segments have been discovered, and characterized by sequence, which AB are response elements operative to confer responsiveness to ligands for several members of the steroid/thyroid superfamily of receptors, for the transcriptional activation and/or repression of promoters in cells. By using transcriptional control regions comprising response elements of the present invention in combination with a functional promoter, it is now possible to provide recombinant DNA vectors containing a gene, the transcription (and, thereby, also expression) of which is under the control of a promoter, the transcriptional activity of which is responsive to ligands for members of the steroid/thyroid superfamily of receptors.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AI US 1991-672530

19910319 (7)

DETD . . . of mouse mammary tumor virus, Herpes simplex thymidine kinase (tk) promoter, basal Simian virus SV-40 promoter, the Drosophila alcohol dehydrogenase (ADH) promoter, and the like. Presently preferred are promoters which require a response element for activity.

IT **67-97-0**, Vitamin D3 6893-02-3, Triiodothyronine

(RARE-containing promoter transactivation by; identification and characterization of steroid/thyroid hormone response elements and use thereof in drug screening)

IT **67-97-0**, Vitamin D3

(RARE-containing promoter transactivation by; identification and characterization of steroid/thyroid hormone response elements and use thereof in drug screening)

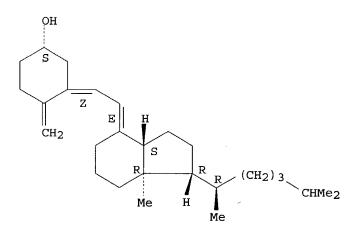
RN 67-97-0 USPATFULL

ECL

CN 9,10-Secocholesta-5,7,10(19)-trien-3-ol, (3β,5Z,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



Exemplary Claim: 1

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ANSWER 3 OF 6 USPATFULL on STN
ΑN
       1999:37090 USPATFULL
       Therapeutic methods utilizing naturally derived bio-active complexes and
TI
       delivery systems therefor
IN
       Danielov, Michael M., 98-25 65th Rd., Apt. 2E, Rego Park, NY, United
       States 11374
       Danielov, Michael M., Rego Park, NY, United States (U.S. individual)
PA
PΙ
       US 5885974
                                19990323
ΑI
       US 1994-350234
                               19941206 (8)
                                                                      < - -
DT
       Utility
FS
       Granted
EXNAM
       Primary Examiner: Criares, Theodore J.
LREP
       Helfgott & Karas, P.C.
CLMN
       Number of Claims: 10
```

DRWN 30 Drawing Figure(s); 30 Drawing Page(s) LN.CNT 2958

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Methods are disclosed for correcting biological information transfer in a patient in need of such therapy which comprise administration to a patient of a composition comprising a therapeutically effective amount of a biocomplex comprising at least one bioactive agent from each of the three informational blocks of biological information transfer, each agent being present in an amount sufficient to correct the biological information transfer of the patient under treatment and resulting in the resumption of normal cell metabolism, said amount being less than the buffering amount of said agent; together with a carrier therefor.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AI US 1994-350234

19941206 (8)

<---

DETD 2. Vasopressin (ADH) was determined using the kits Vasopressin RIA (Buhlman Labor, Switzerland):

RIA (Buhlman Labor, Switzerland); IT 50-14-6, Ergocalciferol 50-23-7, Hydrocortisone β-Estradiol, biological studies 50-81-7, L-Ascorbic acid, biological studies 51-61-6, Dopamine, biological studies 52-39-1, Aldosterone 52-89-1, L-Cysteine hydrochloride 53-59-8, β-NADP 53-84-9, β -NAD 54-47-7, Pyridoxal-5-phosphate 55-31-2, Epinephrine hydrochloride 56-65-5, Adenosine triphosphate, biological 56-81-5D, 1,2,3-Propanetriol, 1,2-diacyl derivs. L-Cystine, biological studies 57-11-4, Octadecanoic acid, biological 57-83-0, Progesterone, biological studies 57-87-4, Ergosterol 57-88-5, Cholesterol, biological studies 58-56-0, Pyridoxine hydrochloride 58-85-5, Biotin 58-95-7, α -Tocopherol acetate 59-30-3, Folic acid, biological studies 60-18-4, L-Tyrosine, biological 60-33-3, 9,12-Octadecadienoic acid (Z,Z)-, biological studies studies 63-91-2, L-Phenylalanine, biological studies 65-71-4, Thymine 66-22-8, Uracil, biological studies 67-03-8, Thiamine hydrochloride 71-30-7, Cytosine 73-22-3, L-Tryptophan, biological studies 73-24-5, Adenine, biological studies 73-40-5, Guanine 79-81-2, Retinol palmitate 85-61-0, Coenzyme A, biological studies 86-01-1, Guanosine triphosphate 96-26-4, Dihydroxyacetone 98-92-0, Nicotinamide 112-85-6, Behenic acid 113-79-1, Arginine vasopressin 117-39-5, 122-32-7, Triolein 123-33-1, Maleic hydrazide 135-16-0, Quercetin Tetrahydrofolic acid 137-08-6, Pantothenic acid hemicalcium salt 145-42-6, Sodium taurocholate 154-87-0, Cocarboxylase 329-56-6, Arterenol hydrochloride 361-09-1, Sodium cholate 363-24-6, Prostaglandin E2 463-40-1, Linolenic acid 481-39-0, Juglone 506-21-8, Linolelaidic acid 506-30-9, Arachidic acid 537-40-6, Trilinolein 551-11-1, Prostaglandin F2a 555-43-1, Tristearin 606-68-8 620-64-4, Triarachidin 745-65-3, Prostaglandin E1 863-57-0, Sodium glycocholate 987-65-5, Adenosine triphosphate disodium 1105-02-8, Corticosterone-21-sulfate 1184-16-3 1340-08-5, salt 1407-47-2, Angiotensin 1731-94-8, Nonadecanoic acid methyl Vitamin P 2566-90-7 2644-64-6, Dipalmitoylphosphatidylcholine 2752-99-0, Trierucin 4537-76-2, Distearoylphosphatidylethanolamine 4537-77-3, Dipalmitoylphosphatidylglycerol 4537-78-4, Distearoylphosphatidylglycerol 4539-70-2, Distearoylphosphatidylcholine 4999-79-5, Estradiol-3-sulfate sodium salt 5681-36-7, Dipalmitoylphosphatidylethanolamine 6064-90-0, Heneicosanoic acid methyl ester 6610-25-9, Arachidonic acid sodium salt 7665-99-8, Cyclic GMP 9001-62-1, Lipase β-Carotene Adrenocorticotropic hormone, biological studies 9002-60-2D, Adrenocorticotropic hormone, 1-24 fragment 9002-64-6, Parathyroid 9002-64-6D, Parathyroid hormone, 1-36 fragment Luteinizing hormone 9002-68-0, Follicle-stimulating hormone 9002-71-5, Thyrotropic hormone 9002-72-6, Somatotropin 9004-10-8, Insulin, biological studies 9004-61-9, Hyaluronic acid Heparin sulfate, biological studies 9007-12-9, Thyrocalcitonin

9007-92-5, Glucagon, biological studies 9015-73-0 9026-43-1, Protein 9041-08-1, Heparin sodium salt 10417-94-4 10529-43-8 11000-17-2, Vasopressin Cholecalciferol sulfate 11061-68-0, Human 11128-99-7, Angiotensin II 12629-01-5, Human growth hormone 14465-68-0 15866-84-9, Adenosine triphosphate calcium salt insulin 13487-42-8 18641-57-1, Tribehenin 18656-38-7, Dimyristoylphosphatidylcholine 20255-95-2, Dimyristoylphosphatidylethanolamine 20290-75-9 24967-93-9, Chondroitin 22251-85-0, Flavin mononucleotide sodium salt sulfate A 24967-94-0, Dermatan sulfate 25322-46-7, Chondroitin sulfate C 26536-13-0, Trinonadecanoin 27964-99-4, Poly-D-lysine hvdrobromide 28845-86-5, 13,16,19-Docosatrienoic acid, (Z,Z,Z)-37221-79-7, Vasoactive 35121-78-9, Prostaglandin I2 28874-58-0 37377-93-8, β-Lipotropin intestinal peptide 37377-93-8D, β-Lipotropin, fragment 37839-81-9, Cyclic AMP sodium salt 40245-60-1, Cyclic GMP sodium salt 41598-07-6, Prostaglandin D2 52910-82-4, Aldosterone-21-hemisuccinate 55672-92-9, Coenzyme A sodium 59392-49-3, Gastric inhibitory peptide 60617-12-1, 60617-12-1D, β -Endorphin, fragment 61361-72-6, Dimyristoylphosphatidylglycerol 61849-14-7, Prostaglandin I2 sodium salt 78392-27-5, Cholecalciferol sulfate sodium salt 80380-39-8, Tri-11-eicosenoin 85166-31-0, D-myo-Inositol-1,4,5-92216-45-0, D-myo-Inositol-2,4,5-triphosphate triphosphate 96012-99-6, Guanosine triphosphate lithium salt 99660-95-4 100775-23-3, Corticosterone-21-sulfate potassium salt 108340-81-4, D-myo-Inositol, 1,4,5-tris(dihydrogen phosphate), hexasodium salt 135271-36-2, D-myo-Inositol-1,4,5-triphosphate potassium salt (bioactive agent-containing biocomplex for correcting biol. information transfer and cell metabolism, and therapeutic use) 50-14-6, Ergocalciferol 10529-43-8, Cholecalciferol sulfate 78392-27-5, Cholecalciferol sulfate sodium salt

(bioactive agent-containing biocomplex for correcting biol. information

Absolute stereochemistry. Rotation (+). Double bond geometry as shown.

transfer and cell metabolism, and therapeutic use)

 $9,10-Secoergosta-5,7,10(19),22-tetraen-3-ol, (3<math>\beta$,5Z,7E,2ZE)- (9CI)

CH₂

E

H

S

Me

R

R

Pr-i

50-14-6 USPATFULL

(CA INDEX NAME)

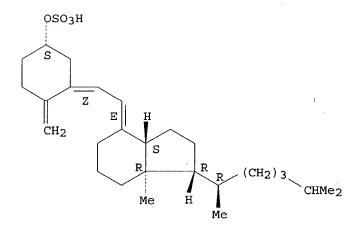
RN

CN

RN 78392-27-5 USPATFULL

Absolute stereochemistry.

Double bond geometry as shown.



Na

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L40
     ANSWER 4 OF 6 USPATFULL on STN
AN
       89:29924 USPATFULL
TI
       Treatment of osteoporosis
IN
       Flora, Lawrence, Fairfield, OH, United States
       The Procter & Gamble Company, Cincinnati, OH, United States (U.S.
PA
       corporation)
                                19890418
PΙ
       US 4822609
ΑI
       US 1986-906725
                                19860912 (6)
                                                                      <--
       Continuation of Ser. No. US 1984-684542, filed on 21 Dec 1984, now
RLI
       abandoned which is a continuation-in-part of Ser. No. US 1984-605541,
       filed on 30 Apr 1984, now abandoned
       Utility
DT
FS
       Granted
EXNAM
       Primary Examiner: Schenkman, Leonard
LREP
       Graff, IV, Milton B., Goldstein, Steven J., Schaeffer, Jack D.
CLMN
       Number of Claims: 16
ECL
       Exemplary Claim: 1
```

DRWN No Drawings

LN.CNT 604

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method for treating or preventing osteoporosis is disclosed. Bone cells are synchronized during a bone cell activating period; bone resorption, which normally follows activation, is inhibited using a polyphosphonate; bone formation is allowed to occur in the rest period during which nutrient supplements may be administered to the patient. The method shortens the natural cycle time of bone formation/resorption, resulting in a faster bone build-up.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

PI US 4822609

19890418

<--

AI US 1986-906725

19860912 (6)

<--

IT 2809-21-4 10596-23-3 40391-99-9 66376-36-1

79778-41-9

(osteoporosis treatment by bone cell-activating agents and)

IT 51-48-9, biological studies 363-24-6 6893-02-3 9002-64-6

16984-48-8, biological studies 19356-17-3 32222-06-3

(osteoporosis treatment by bone resorption-inhibiting polyphosphonates and)

IT 40391-99-9 66376-36-1

(osteoporosis treatment by bone cell-activating agents and)

RN 40391-99-9 USPATFULL

CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX NAME)

OH

$$|$$

 $H_2O_3P-C-CH_2-CH_2-NH_2$
 $|$
 PO_3H_2

RN 66376-36-1 USPATFULL

CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)

IT 19356-17-3 32222-06-3

(osteoporosis treatment by bone resorption-inhibiting polyphosphonates and)

RN 19356-17-3 USPATFULL

CN 9,10-Secocholesta-5,7,10(19)-triene-3,25-diol, (3β,5Z,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 32222-06-3 USPATFULL CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, (1α,3β,5Z,7E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+). Double bond geometry as shown.

ANSWER 5 OF 6 USPATFULL on STN

89:19032 USPATFULL

L40 AN

```
ΤI
       Kit for use in the treatment of osteoporosis
       Uchtman, Vernon A., Cincinnati, OH, United States
IN
PA
       The Procter & Gamble Company, Cincinnati, OH, United States (U.S.
       corporation)
       US 4812311
PI
                                19890314
                                                                      <---
       US 1986-906859
AΙ
                                19860912 (6)
                                                                      <---
DCD
       20060314
RLI
       Continuation of Ser. No. US 1984-684560, filed on 21 Dec 1984, now
       abandoned which is a continuation-in-part of Ser. No. US 1984-605540,
       filed on 30 Apr 1984, now abandoned
DT
       Utility
FS
       Granted
EXNAM
       Primary Examiner: Schenkman, Leonard
LREP
       Graff, IV, Milton B., Goldstein, Steven J., Schaeffer, Jack D.
CLMN
       Number of Claims: 17
ECL
       Exemplary Claim: 1
DRWN
       No Drawings
LN.CNT 773
```

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A kit for use in the treatment of osteoporosis is disclosed. The kit comprises a bone cell activating compound, a bone resorption inhibiting polyphosphonate, and a nutrient supplement or placebo, for sequential administration.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

US 4812311

19890314

AI US 1986-906859

PΙ

IT

19860912 (6)

. - -

51-48-9, biological studies 363-24-6 1406-16-2 2809-21-4 6893-02-3 7414-83-7 7440-70-2, biological studies 10596-23-3 12583-68-5 13598-36-2D, derivs. 14265-44-2, biological studies

16984-48-8, biological studies 19356-17-3 32222-06-3

40391-99-9 66376-36-1 79778-41-9

(osteoporosis treatment with, regimen kit for)

IT 19356-17-3 32222-06-3 40391-99-9

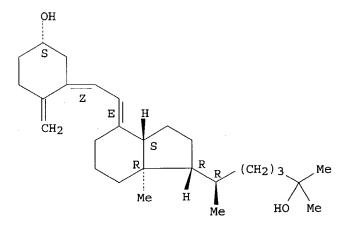
66376-36-1

(osteoporosis treatment with, regimen kit for)

RN 19356-17-3 USPATFULL

CN 9,10-Secocholesta-5,7,10(19)-triene-3,25-diol, (3β,5Z,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 32222-06-3 USPATFULL

CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, $(1\alpha,3\beta,5Z,7E)$ -(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+). Double bond geometry as shown.

RN 40391-99-9 USPATFULL

CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX NAME)

$$^{\mathrm{OH}}$$
 $^{\mathrm{H}_{2}\mathrm{O}_{3}\mathrm{P}-\mathrm{CH}_{2}-\mathrm{CH}_{2}-\mathrm{NH}_{2}}$
 $^{\mathrm{H}_{2}\mathrm{O}_{3}\mathrm{H}_{2}-\mathrm{CH}_{2}-\mathrm{NH}_{2}-\mathrm{NH}_{2}}$

RN 66376-36-1 USPATFULL

ANSWER 6 OF 6 USPATFULL on STN

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)

L40

```
89:19025 USPATFULL
AN
       Treatment of osteoporosis
ΤI
       Anderson, Colin, Lambeth, Canada
IN
       Flora, Lawrence, Fairfield, OH, United States
       The Procter & Gamble Company, Cincinnati, OH, United States (U.S.
PA
       corporation)
       US 4812304
PΙ
                               19890314
                                                                      <---
ΑI
       US 1986-906858
                               19860912 (6)
                                                                      <---
DCD
       20060314
       Continuation of Ser. No. US 1984-684541, filed on 21 Dec 1984, now
RLI
       abandoned which is a continuation-in-part of Ser. No. US 1984-605539,
       filed on 30 Apr 1984, now abandoned
DT
       Utility
FS
       Granted
      Primary Examiner: Schenkman, Leonard
EXNAM
       Graff, IV, Milton B., Goldstein, Steven J., Schaeffer, Jack D.
LREP
CLMN
       Number of Claims: 14
ECL
       Exemplary Claim: 1
DRWN
       No Drawings
LN.CNT 619
```

AB A method for treating or preventing osteoporosis is disclosed. Bone cells are synchronized during a bone cell activating period; bone resorption, which normally follows activation, is inhibited using a polyphosphonate; bone formation is allowed to occur in the rest period during which nutrient supplements may be administered to the patient.

CAS INDEXING IS AVAILABLE FOR THIS PATENT. US 4812304 19890314 <---US 1986-906858 19860912 (6) <--AI2809-21-4 10596-23-3 **40391-99-9 66376-36-1** IT 79778-41-9 (bone absorption-inhibiting agent, in osteoporosis treatment) 51-48-9, biological studies 363-24-6 6893-02-3 7414-83-7 IT 16984-48-8, biological 7681-49-4, biological studies 9002-64-6 studies 19356-17-3 32222-06-3 (bone cell-activating agent, in osteoporosis treatment) IT40391-99-9 66376-36-1 (bone absorption-inhibiting agent, in osteoporosis treatment) 40391-99-9 USPATFULL RNPhosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX NAME) CN

$$\begin{array}{c} \text{OH} \\ | \\ \text{H}_2\text{O}_3\text{P--}\text{C--}\text{CH}_2\text{--}\text{CH}_2\text{--}\text{NH}_2 \\ | \\ \text{PO}_3\text{H}_2 \end{array}$$

RN 66376-36-1 USPATFULL CN Phosphonic acid, (4-amino-1-hydroxybutylidene)bis- (9CI) (CA INDEX NAME)

$$^{OH}_{|}$$
 $_{|}$
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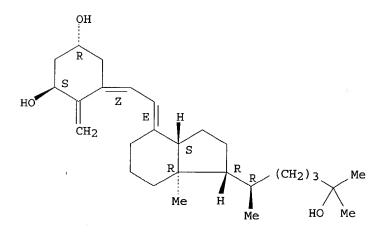
IT 19356-17-3 32222-06-3

(bone cell-activating agent, in osteoporosis treatment)

RN 19356-17-3 USPATFULL

CN 9,10-Secocholesta-5,7,10(19)-triene-3,25-diol, $(3\beta,5Z,7E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+). Double bond geometry as shown.



=> d bib abs hitstr

```
ANSWER 1 OF 1 USPATFULL on STN
AN
       2002:250793 USPATFULL
TI
       Targeted therapeutic delivery of vitamin D compounds
IN
       Mazess, Richard B., Madison, WI, UNITED STATES
       Bishop, Charles W., Madison, WI, UNITED STATES
PI
       US 2002136731
                          A1
                               20020926
ΑI
       US 2000-402636
                          A1
                               20000426 (9)
       WO 1998-US2899
                               19980213
DT
       Utility
FS
       APPLICATION
       Teresa J Welch, Michael Best & Friedrich, One South Pinckney Street
LREP
       Suite 700, PO Box 1806, Madison, WI, 53701-1806
CLMN
       Number of Claims: 40
ECL
       Exemplary Claim: 1
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DRWN 9 Drawing Page(s)

LN.CNT 1272

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The present invention is directed to a conjugate which includes at least one vitamin D moiet thereof and at least one targeting molecule moiety to pharmaceutical compositions of the conjugate. and to methods for using the conjugate for target- specific delivery of vitamin D or analogs thereof to tissues in need thereof. When a particularly preferred form is administered to a patient, the targeting molecule component of the conjugate of this invention seeks out and binds to a tissue of interest, such as bone or tuinor tissue, where the vitamin D has a therapeutic effect.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 211865-88-2P 211865-89-3P 211865-90-6P

211865-97-3P 211865-98-4P 211865-99-5P

211866-02-3P 211866-03-4P 211866-04-5P

211866-12-5P 211866-13-6P 211866-16-9P

211866-17-0P 211866-20-5P 211866-21-6P

(preparation of vitamin D2 analog-bisphosphonate conjugates for targeted delivery)

RN 211865-88-2 USPATFULL

CN 9,10-Secoergosta-5,7,10(19),22-tetraen-24-ol, 1,3-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-, [4,4-bis[bis(1-methylethoxy)phosphinyl]butyl]carbamate, $(1\alpha,3\beta,5E,7E,22E)$ -(9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

PAGE 1-A

PAGE 1-B

CN 9,10-Secoergosta-5,7,10(19),22-tetraene-1,3,24-triol, 24-[[4,4-bis[bis(1-methylethoxy)phosphinyl]butyl]carbamate], $(1\alpha,3\beta,5E,7E,22E)$ (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

PAGE 1-A

PAGE 1-B

CN

RN 211865-90-6 USPATFULL

9,10-Secoergosta-5,7,10(19),22-tetraene-1,3,24-triol, 24-[(4,4-diphosphonobutyl)carbamate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 211865-97-3 USPATFULL

CN 9,10-Secoergosta-5,7,10(19),22-tetraen-1-ol, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-24-(methoxymethoxy)-, [4,4-bis[bis(1-methylethoxy)phosphinyl]butyl]carbamate, $(1\alpha,3\beta,5E,7E,22E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

PAGE 1-A

PAGE 1-B

CN

RN 211865-98-4 USPATFULL

9,10-Secoergosta-5,7,10(19),22-tetraene-1,3-diol, 24-(methoxymethoxy)-, 1-[[4,4-bis[bis(1-methylethoxy)phosphinyl]butyl]carbamate], $(1\alpha,3\beta,5E,7E,22E)$ - (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

RN 211865-99-5 USPATFULL

CN 9,10-Secoergosta-5,7,10(19),22-tetraene-1,3,24-triol, 1-[(4,4-diphosphonobutyl)carbamate], (1α ,3 β ,5E,7E,22E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

PAGE 1-A

$$H_{2}O_{3}P$$
 $(CH_{2})_{3}$
 H_{N}
 O
 S
 E
 E
 H_{N}
 O
 Me
 Me
 Me
 Me
 Me
 Me

PAGE 1-B

__Pr-i

RN 211866-02-3 USPATFULL

CN 9,10-Secoergosta-5,7,10(19),22-tetraen-3-ol, 1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-24-(methoxymethoxy)-,
 [4,4-bis[bis(1-methylethoxy)phosphinyl]butyl]carbamate,
 (1α,3β,5E,7E,22E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

PAGE 1-A

PAGE 1-B

OMe

RN 211866-03-4 USPATFULL CN 9,10-Secoergosta-5,7,10

9,10-Secoergosta-5,7,10(19),22-tetraene-1,3-diol, 24-(methoxymethoxy)-, 3-[[4,4-bis[bis(1-methylethoxy)phosphinyl]butyl]carbamate], $(1\alpha,3\beta,5E,7E,22E)$ - (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

_ OMe

RN 211866-04-5 USPATFULL

CN 9,10-Secoergosta-5,7,10(19),22-tetraene-1,3,24-triol, 3-[(4,4-diphosphonobutyl)carbamate], $(1\alpha,3\beta,5E,7E,22E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

HO. S E E H HO. Me H R E S
$$\operatorname{Pr-i}$$
 Me $\operatorname{H}_{2}\operatorname{O_3P}$

RN 211866-12-5 USPATFULL

CN 9,10-Secocholesta-5,7,10(19)-trien-1-ol, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-25-[(tetrahydro-2H-pyran-2-yl)oxy]-, [4,4-bis[bis(1-methylethoxy)phosphinyl]butyl]carbamate, $(1\alpha,3\beta,5Z,7E)$ - (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

RN 211866-13-6 USPATFULL

CN _9,10-Secocholesta-5,7,10(19)-triene-1,3-diol, 25-[(tetrahydro-2H-pyran-2-yl)oxy]-, 1-[[4,4-bis[bis(1-methylethoxy)phosphinyl]butyl]carbamate], $(1\alpha,3\beta,5Z,7E)$ - (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

RN 211866-16-9 USPATFULL

9,10-Secocholesta-5,7,10(19)-trien-3-ol, 1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-25-[(tetrahydro-2H-pyran-2-yl)oxy]-,
 [4,4-bis[bis(1-methylethoxy)phosphinyl]butyl]carbamate,
 (1α,3β,5Z,7E)- (9CI) (CA INDEX NAME)

RN 211866-17-0 USPATFULL

CN 9,10-Secocholesta-5,7,10(19)-triene-1,3-diol, 25-[(tetrahydro-2H-pyran-2-yl)oxy]-, 3-[[4,4-bis[bis(1-methylethoxy)phosphinyl]butyl]carbamate], $(1\alpha,3\beta,5Z,7E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 211866-20-5 USPATFULL

CN 9,10-Secocholesta-5,7,10(19)-trien-25-ol, 1,3-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-, [2,2-bis[bis(1-methylethoxy)phosphinyl]ethyl]carbamate, $(1\alpha,3\beta,5Z,7E)$ - (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

CN

RN 211866-21-6 USPATFULL

9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 25-[2,2-bis[bis(1-methylethoxy)phosphinyl]ethyl]carbamate, $(1\alpha,3\beta,5Z,7E)$ - (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

─opr-i

IT 211865-91-7P 211866-00-1P 211866-05-6P 211866-14-7P 211866-18-1P 211866-22-7P

(preparation of vitamin D2 analog-bisphosphonate conjugates for targeted delivery)

RN 211865-91-7 USPATFULL

CN 9,10-Secoergosta-5,7,10(19),22-tetraene-1,3,24-triol, 24-[(4,4-diphosphonobutyl)carbamate], $(1\alpha,3\beta,5Z,7E,22E)$ - (9CI) (CA INDEX NAME)

RN 211866-00-1 USPATFULL

CN 9,10-Secoergosta-5,7,10(19),22-tetraene-1,3,24-triol, 1-[(4,4-diphosphonobutyl)carbamate], $(1\alpha,3\beta,5Z,7E,22E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

PAGE 1-A

$$H_{2}O_{3}P$$
 CH_{2}
 CH_{2

PAGE 1-B

RN 211866-05-6 USPATFULL

CN 9,10-Secoergosta-5,7,10(19),22-tetraene-1,3,24-triol, 3-[(4,4-diphosphonobutyl)carbamate], $(1\alpha,3\beta,5Z,7E,22E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 211866-14-7 USPATFULL

CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 1-[(4,4-diphosphonobutyl)carbamate], $(1\alpha,3\beta,5Z,7E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

PAGE 1-A

$$H_{2}O_{3}P$$
 $(CH_{2})_{3}$
 N
 $H_{2}O_{3}P$
 $(CH_{2})_{3}$
 N
 $H_{2}O_{3}P$
 $(CH_{2})_{3}$
 N
 $H_{2}O_{3}P$
 $(CH_{2})_{3}$
 $(CH_{2})_{3}$
 $(CH_{2})_{3}$
 $(CH_{2})_{3}$
 $(CH_{2})_{3}$
 $(CH_{2})_{3}$
 $(CH_{2})_{3}$

PAGE 1-B

Me

RN 211866-18-1 USPATFULL

CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 3-[(4,4-diphosphonobutyl)carbamate], $(1\alpha,3\beta,5Z,7E)$ - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 211866-22-7 USPATFULL

CN 9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, 25-[(2,2-diphosphonoethyl)carbamate], $(1\alpha,3\beta,5Z,7E)$ - (9CI) (CA INDEX NAME)

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L3 STR
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L5 4726 S L3 FUL
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L21 6 S L12, L20 SEL RN

L17 L18

L19

L20

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L25
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L26
           8028 S L24-L26
L27
L28
            111 S L27 AND L2
L29
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L35
L36
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L38
              7 S L38 NOT HYDROXYLASE/TI
L39
L40
              6 S L39 NOT P450/TI
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L41

1 S L34 NOT L40